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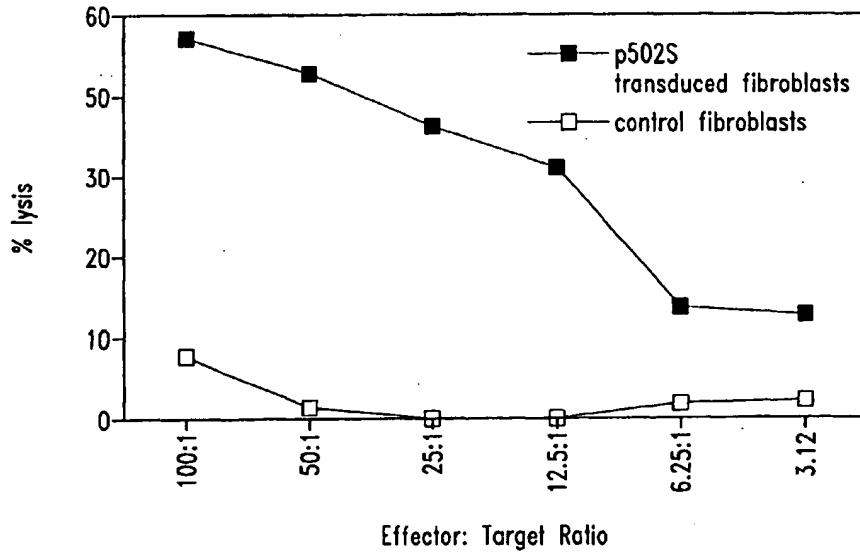
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(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



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(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.



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COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

5 TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for 10 prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress 15 inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but 20 these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate 25 with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

30 SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the

diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate-specific protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, 5 the polypeptide comprises at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 10 381, 382,384-476, 524, 526, 530, 531, 533, 535 and 536; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the 15 sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-550.

15 The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate-specific protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

20 Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

25 The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate-specific protein; and (b) a physiologically acceptable carrier. In certain embodiments, the present invention provides monoclonal antibodies that specifically bind to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 522 and 541-550, together with 30 monoclonal antibodies comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

5 Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

10 Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

15 Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

20 The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

25 Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

30 Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate-specific protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

10 Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain

embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that

5 hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b)

10 detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as

15 monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed

20 herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The

25 percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of γ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure

30 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

5 Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

10 Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

15 Figures 6A and 6B are graphs illustrating the specificity of a CD8⁺ cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a ⁵¹Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

20 Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

25 Figure 11 shows the results of an ELISA assay of antibody specificity to P501S peptides.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12

SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16

30 SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1

SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9

SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4

SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12
5 SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862
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SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19
10 SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19
SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25
SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25
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SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24
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SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14
SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12
SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
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SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48
SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55
SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
30 SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858
SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861

SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864
SEQ ID NO: 41 is the determined cDNA sequence for P5
SEQ ID NO: 42 is the determined cDNA sequence for P8
SEQ ID NO: 43 is the determined cDNA sequence for P9
5 SEQ ID NO: 44 is the determined cDNA sequence for P18
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SEQ ID NO: 46 is the determined cDNA sequence for P29
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SEQ ID NO: 63 is the determined cDNA sequence for P76
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SEQ ID NO: 66 is the determined cDNA sequence for P68
SEQ ID NO: 67 is the determined cDNA sequence for P80
SEQ ID NO: 68 is the determined cDNA sequence for P82
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SEQ ID NO: 71 is the determined cDNA sequence for V1-3692

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SEQ ID NO: 74 is the determined cDNA sequence for R1-2330
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SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781
SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785
SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787
15 SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796
SEQ ID NO: 87 is the determined cDNA sequence for 1I-4807
SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810
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SEQ ID NO: 99 is the determined cDNA sequence for 1D-4297
SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309
30 SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278
SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288
SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283

SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304
SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296
SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280
SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S)

5
SEQ ID NO: 108 is the predicted amino acid sequence for F1-12
SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17
SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 (also referred to as P501S)
SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as
10 P503S)
SEQ ID NO: 112 is the predicted amino acid sequence for J1-17
SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also referred to as P501S)
SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also referred to as P503S)
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SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con

SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev

SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd

SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev

15 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd

SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev

SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd

SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev

SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd

20 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev

SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd

SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev

SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev

SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd

25 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev

SEQ ID NO: 223 is the determined cDNA sequence for P509S

SEQ ID NO: 224 is the determined cDNA sequence for P510S

SEQ ID NO: 225 is the determined cDNA sequence for P703DE5

SEQ ID NO: 226 is the determined cDNA sequence for 9-A11

30 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6

SEQ ID NO: 228 is the determined cDNA sequence for 8-H7

SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13

SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23
SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25
5 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35
SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38
10 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41
SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42
SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45
15 SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56
SEQ ID NO: 247 is the determined cDNA sequence for PTPN64
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65
20 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84
SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86
25 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1
SEQ ID NO: 257 is the determined cDNA sequence for JP1F2
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2
30 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3

SEQ ID NO: 262 is the determined cDNA sequence for JP1A4
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6
5 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5
SEQ ID NO: 267 is the determined cDNA sequence for JP1A6
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9
10 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10
SEQ ID NO: 272 is the determined cDNA sequence for JP1A9
SEQ ID NO: 273 is the determined cDNA sequence for JP1F12
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11
15 SEQ ID NO: 276 is the determined cDNA sequence for JP1C11
SEQ ID NO: 277 is the determined cDNA sequence for JP1C12
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2
20 SEQ ID NO: 281 is the determined cDNA sequence for JP8H1
SEQ ID NO: 282 is the determined cDNA sequence for JP8H2
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3
25 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4
SEQ ID NO: 287 is the determined cDNA sequence for JP8B6
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8
30 SEQ ID NO: 291 is the determined cDNA sequence for JP8C7
SEQ ID NO: 292 is the determined cDNA sequence for JP8D7
SEQ ID NO: 293 is the determined cDNA sequence for P8D8

SEQ ID NO: 294 is the determined cDNA sequence for JP8E7

SEQ ID NO: 295 is the determined cDNA sequence for JP8F8

SEQ ID NO: 296 is the determined cDNA sequence for JP8G8

SEQ ID NO: 297 is the determined cDNA sequence for JP8B10

5 SEQ ID NO: 298 is the determined cDNA sequence for JP8C10

SEQ ID NO: 299 is the determined cDNA sequence for JP8E9

SEQ ID NO: 300 is the determined cDNA sequence for JP8E10

SEQ ID NO: 301 is the determined cDNA sequence for JP8F9

SEQ ID NO: 302 is the determined cDNA sequence for JP8H9

10 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12

SEQ ID NO: 304 is the determined cDNA sequence for JP8E11

SEQ ID NO: 305 is the determined cDNA sequence for JP8E12

SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12

SEQ ID NO: 307 is the determined cDNA sequence for P711P

15 SEQ ID NO: 308 is the determined cDNA sequence for P712P

SEQ ID NO: 309 is the determined cDNA sequence for CLONE23

SEQ ID NO: 310 is the determined cDNA sequence for P774P

SEQ ID NO: 311 is the determined cDNA sequence for P775P

SEQ ID NO: 312 is the determined cDNA sequence for P715P

20 SEQ ID NO: 313 is the determined cDNA sequence for P710P

SEQ ID NO: 314 is the determined cDNA sequence for P767P

SEQ ID NO: 315 is the determined cDNA sequence for P768P

SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes

SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5

25 SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5

SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26

SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26

SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23

SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23

30 SEQ ID NO: 332 is the determined full length cDNA sequence for P509S

SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)

SEQ ID NO: 334 is the determined cDNA sequence for P714P

SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)

SEQ ID NO: 336 is the predicted amino acid sequence for P705P

SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10

SEQ ID NO: 338 is the amino acid sequence of the peptide p5

5 SEQ ID NO: 339 is the predicted amino acid sequence of P509S

SEQ ID NO: 340 is the determined cDNA sequence for P778P

SEQ ID NO: 341 is the determined cDNA sequence for P786P

SEQ ID NO: 342 is the determined cDNA sequence for P789P

SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo

10 sapiens MM46 mRNA

SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA

SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin

15 SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)

SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)

SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo

20 sapiens phosphoglucomutase-related protein (PGMRP)

SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40

SEQ ID NO: 350 is the determined cDNA sequence for P777P

SEQ ID NO: 351 is the determined cDNA sequence for P779P

25 SEQ ID NO: 352 is the determined cDNA sequence for P790P

SEQ ID NO: 353 is the determined cDNA sequence for P784P

SEQ ID NO: 354 is the determined cDNA sequence for P776P

SEQ ID NO: 355 is the determined cDNA sequence for P780P

SEQ ID NO: 356 is the determined cDNA sequence for P544S

30 SEQ ID NO: 357 is the determined cDNA sequence for P745S

SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984

SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

5 SEQ ID NO: 364 is the determined cDNA sequence for P781P

SEQ ID NO: 365 is the determined cDNA sequence for P785P

SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.

10 SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.

SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 15 374.

SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.

SEQ ID NO: 381 is the determined cDNA sequence for B716P.

SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.

20 SEQ ID NO: 383 is the predicted amino acid sequence for P711P.

SEQ ID NO: 384 is the cDNA sequence for P1000C.

SEQ ID NO: 385 is the cDNA sequence for CGI-82.

SEQ ID NO: 386 is the cDNA sequence for 23320.

SEQ ID NO: 387 is the cDNA sequence for CGI-69.

25 SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.

SEQ ID NO: 389 is the cDNA sequence for 23379.

SEQ ID NO: 390 is the cDNA sequence for 23381.

SEQ ID NO: 391 is the cDNA sequence for KIAA0122.

SEQ ID NO: 392 is the cDNA sequence for 23399.

30 SEQ ID NO: 393 is the cDNA sequence for a previously identified gene.

SEQ ID NO: 394 is the cDNA sequence for HCLBP.

SEQ ID NO: 395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.

SEQ ID NO:399 is the cDNA sequence for hTGR.

5 SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

SEQ ID NO:404 is the cDNA sequence for 22550.

10 SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553.

SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

15 SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.

20 SEQ ID NO:415 is the cDNA sequence for 22572.

SEQ ID NO:416 is the cDNA sequence for 22573.

SEQ ID NO:417 is the cDNA sequence for 22573.

SEQ ID NO:418 is the cDNA sequence for 22575.

SEQ ID NO:419 is the cDNA sequence for 22580.

25 SEQ ID NO:420 is the cDNA sequence for 22581.

SEQ ID NO:421 is the cDNA sequence for 22582.

SEQ ID NO:422 is the cDNA sequence for 22583.

SEQ ID NO:423 is the cDNA sequence for 22584.

SEQ ID NO:424 is the cDNA sequence for 22585.

30 SEQ ID NO:425 is the cDNA sequence for 22586.

SEQ ID NO:426 is the cDNA sequence for 22587.

SEQ ID NO:427 is the cDNA sequence for 22588.

SEQ ID NO:428 is the cDNA sequence for 22589.

SEQ ID NO:429 is the cDNA sequence for 22590.

SEQ ID NO:430 is the cDNA sequence for 22591.

SEQ ID NO:431 is the cDNA sequence for 22592.

5 SEQ ID NO:432 is the cDNA sequence for 22593.

SEQ ID NO:433 is the cDNA sequence for 22594.

SEQ ID NO:434 is the cDNA sequence for 22595.

SEQ ID NO:435 is the cDNA sequence for 22596.

SEQ ID NO:436 is the cDNA sequence for 22847.

10 SEQ ID NO:437 is the cDNA sequence for 22848.

SEQ ID NO:438 is the cDNA sequence for 22849.

SEQ ID NO:439 is the cDNA sequence for 22851.

SEQ ID NO:440 is the cDNA sequence for 22852.

SEQ ID NO:441 is the cDNA sequence for 22853.

15 SEQ ID NO:442 is the cDNA sequence for 22854.

SEQ ID NO:443 is the cDNA sequence for 22855.

SEQ ID NO:444 is the cDNA sequence for 22856.

SEQ ID NO:445 is the cDNA sequence for 22857.

SEQ ID NO:446 is the cDNA sequence for 23601.

20 SEQ ID NO:447 is the cDNA sequence for 23602.

SEQ ID NO:448 is the cDNA sequence for 23605.

SEQ ID NO:449 is the cDNA sequence for 23606.

SEQ ID NO:450 is the cDNA sequence for 23612.

SEQ ID NO:451 is the cDNA sequence for 23614.

25 SEQ ID NO:452 is the cDNA sequence for 23618.

SEQ ID NO:453 is the cDNA sequence for 23622.

SEQ ID NO:454 is the cDNA sequence for folate hydrolase.

SEQ ID NO:455 is the cDNA sequence for LIM protein.

SEQ ID NO:456 is the cDNA sequence for a known gene.

30 SEQ ID NO:457 is the cDNA sequence for a known gene.

SEQ ID NO:458 is the cDNA sequence for a previously identified gene.

SEQ ID NO:459 is the cDNA sequence for 23045.

SEQ ID NO:460 is the cDNA sequence for 23032.

SEQ ID NO:461 is the cDNA sequence for 23054.

SEQ ID NO:462-467 are cDNA sequences for known genes.

SEQ ID NO:468-471 are cDNA sequences for P710P.

5 SEQ ID NO:472 is a cDNA sequence for P1001C.

SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).

SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).

10 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).

SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).

SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO:

15 474.

SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.

20 SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO:

25 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

30 SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for 5 the anti-P503S monoclonal antibody JA1.

SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for 10 the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P. SEQ ID NO: 15 524 is the putative full-length cDNA sequence of P703P.

SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.

SEQ ID NO: 526 is the full-length cDNA sequence for P790P.

SEQ ID NO: 527 is the predicted amino acid sequence for P790P.

SEQ ID NO: 528 & 529 are PCR primers.

SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.

SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.

SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.

SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.

SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.

SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.

SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.

SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.

SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.

SEQ ID NO: 539 is the peptide P501S-370.

SEQ ID NO: 540 is the peptide P501S-376.

SEQ ID NO: 541-550 are epitopes of P501S.

SEQ ID NO: 551 corresponds to amino acids 543-553 of P501S.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate-specific polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate-specific protein or a variant thereof. A "prostate-specific protein" is a protein that is expressed in normal prostate and/or prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a non-prostate normal tissue, as determined using a representative assay provided herein. Certain prostate-specific proteins are proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate-specific proteins. Sequences of polynucleotides encoding certain prostate-specific proteins, or portions thereof, are provided in SEQ ID NOS:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Sequences of polypeptides comprising at least a portion of a prostate-specific protein are provided in SEQ ID NOS:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

PROSTATE-SPECIFIC PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate-specific protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred

polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate-specific protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate-specific protein. Polynucleotides complementary to any such sequences are also 5 encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the 10 present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate-specific protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions 15 and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate-specific protein or a portion thereof. The 20 term "variants" also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local 25 regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the 30 Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices

for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) *Unified Approach to Alignment and Phylogenies* pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the “percentage of sequence identity” is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate-specific protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such

as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example,

5 a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate-specific than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997).

10 Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate-specific cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

15 An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate-specific cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes.

20 Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into

a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments; using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally 5 performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (see Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence 15 and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the 20 use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

25 In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

30 Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate-specific protein are provided in SEQ ID NO:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536.

Isolation of these polynucleotides is described below. Each of these prostate-specific proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. 5 Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate-specific protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain 10 portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate-specific polypeptide, and administering the transfected cells to the patient).

15 A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a protein. Antisense technology can be used to control gene expression 20 through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., *In Huber and Carr, Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of 25 the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3'

ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiester linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

5 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector
10 will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

15 Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there
20 are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). The polynucleotides may also be administered as naked plasmid vectors.
25 Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary
skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane
30 vesicle). The preparation and use of such systems is well known in the art.

PROSTATE-SPECIFIC POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate-specific protein or a variant thereof, as described herein. As noted above, a "prostate-specific protein" is a protein that is expressed by normal prostate and/or prostate tumor cells. Proteins that are prostate-specific proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate-specific protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate-specific protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the

immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ^{125}I -labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate-specific protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate-specific protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino

acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques.

- 10 Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells.
- 15 Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed
- 20 to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See 25 Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that 30 comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known prostate-specific protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner),

preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted
5 to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly,
10 DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component
15 polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be
20 chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker
25 sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions
30 that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are

located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the LytA gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see *Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its

original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector 5 that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate-specific protein. As used herein, an 10 antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate-specific protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate-specific protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding 15 constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

20 Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate-specific protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals 25 without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number 30 of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Most preferably, antibodies employed in the inventive methods have the ability to induce lysis of tumor cells by activation of complement and mediation of antibody-dependent cellular cytotoxicity (ADCC). Antibodies of different classes and subclasses differ in these properties. For example, mouse antibodies of the IgG2a and IgG3 classes are capable of activating serum complement upon binding to target cells which express the antigen against which the antibodies were raised, and can mediate ADCC.

Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells

and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are 5 selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. 10 Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

The preparation of mouse and rabbit monoclonal antibodies that specifically bind to 15 polypeptides of the present invention is described in detail below. However, the antibodies of the present invention are not limited to those derived from mice. Human antibodies may also be employed in the inventive methods and may prove to be preferable. Such antibodies can be obtained using human hybridomas as described by Cote *et al.* (*Monoclonal Antibodies and Cancer Therapy*, Alan R. Lisa, p. 77, 1985). The present invention also encompasses antibodies made by 20 recombinant means such as chimeric antibodies, wherein the variable region and constant region are derived from different species, and CDR-grafted antibodies, wherein the complementarity determining region is derived from a different species, as described in US Patents 4,816,567 and 5,225,539. Chimeric antibodies may be prepared by splicing genes for a mouse antibody molecule having a desired antigen specificity together with genes for a human antibody molecule having the 25 desired biological activity, such as activation of human complement and mediation of ADCC (*Morrison et al. Proc. Natl. Acad. Sci. USA* 81:6851, 1984; *Neuberger et al. Nature* 312:604, 1984; *Takeda et al. Nature* 314:452, 1985).

Within certain embodiments, the use of antigen-binding fragments of antibodies may 30 be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*,

Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, 5 drugs, toxins, and derivatives thereof. Preferred radionuclides include ⁹⁰Y, ¹²³I, ¹²⁵I, ¹³¹I, ¹⁸⁶Re, ¹⁸⁸Re, ²¹¹At, and ²¹²Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

10 A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid 15 halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

20 Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional 25 groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized 25 carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

30 Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to

Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

5 It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or
10 linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent
15 No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating
20 compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of
25 a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

30 Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate-specific protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral

blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from Nexell Therapeutics Inc., Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated 5 humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate-specific polypeptide, polynucleotide encoding a prostate-specific polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate-specific 10 polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate-specific polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a 15 variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell 20 proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate-specific polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of 25 the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN- γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate-specific polypeptide, polynucleotide or polypeptide-expressing APC may be CD4 $^{+}$ and/or CD8 $^{+}$. Prostate-specific protein-specific T cells may be expanded using 30 standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a prostate-specific polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate-specific polypeptide, or a short peptide 5 corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate-specific polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate-specific protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

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PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds 15 and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally 20 described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be 25 present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression 30 systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression

in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; 10 WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Käss-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and 15 Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the 20 DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary 20 depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid 25 carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA 30

or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example,

an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent 5 adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release 10 formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release 15 formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical 20 compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the 25 antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or 30 progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (see Timmerman and Levy,

Ann. Rev. Med. 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take-up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a prostate-specific protein (or portion or other variant thereof) such that the prostate-specific polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection

that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells 5 with the prostate-specific polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of 10 the polypeptide.

CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical 15 compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. 20 Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react 25 against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not 30 necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer

cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate 5 antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in* 10 *vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, 15 fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies 20 have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back 25 into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitory, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established 30 using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered

over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate-specific protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more prostate-specific proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer.

In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, 5 *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized 10 on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, 15 protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full 20 length prostate-specific proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or 25 disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" 30 refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a

membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of 5 binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the 10 binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may 15 be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The 20 amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 25 20TM (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. 30 Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by

assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20TM. The second antibody, which contains 5 a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of 10 time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group 15 (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a 20 signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is 25 determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true 30 positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along

the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate-specific polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate-specific protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate-specific protein in a biological sample. Within certain methods, a biological sample comprising CD4 $^{+}$ and/or CD8 $^{+}$ T cells isolated from a patient is incubated with a prostate-specific polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that

expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may
5 be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate-specific polypeptide (*e.g.*, 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate-specific polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater
10 and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate-specific protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to
15 amplify a portion of a prostate-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate-specific protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate-specific protein may be used in a hybridization
20 assay to detect the presence of polynucleotide encoding the protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate-specific protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in
25 length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15
30 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Techniques for both PCR based assays and hybridization assays

are well known in the art (see, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, 5 and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction 10 may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer 15 may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or 20 polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such 25 applications.

As noted above, to improve sensitivity, multiple prostate-specific protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or 30 alternatively, assays for proteins provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate-specific protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate-specific protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate-specific protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate-specific protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

EXAMPLE 1

5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate 10 tumor poly A⁺ RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA was then purified using a Qiagen oligotex spin column mRNA 15 purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into 20 ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained 1.64×10^7 25 independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained 3.3×10^6 independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

30 cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as

follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H₂O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H₂O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H₂O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H₂O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 µg each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA

library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated

clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 5 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further 10 analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the 15 identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 20 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to 25 those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

30 cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni,

Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and 10 P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S 15 are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively.

EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

20 Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using 25 Trizol reagent as described above. First strand synthesis was carried out using 1-2 µg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed 30 using β-actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β-actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for each

reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue
5 (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found
10 to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other
15 tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of
20 prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

25 RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH
30 prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney,

but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following 5 normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues 10 tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in 15 normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in 20 prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and 25 expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney). The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was 30 found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis 10 of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, 15 and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

20

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with 25 ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). 30 DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences 5 for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the 10 isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones 15 (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161- 20 170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid 25 sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary 25 (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a 30 portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of

2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in 5 prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, 10 substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The 15 determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 20 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array 25 technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, 30 colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity 5 to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA 10 sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of 15 P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. The putative full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 525.

20 Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 25 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal 30 prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the 5 cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence 10 being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no 15 significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

Further studies on P775P resulted in the isolation of four additional sequences (SEQ 20 ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479. 25 The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483.

Subsequent studies led to the identification of a genomic region on chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the 30 genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led

to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

EXAMPLE 4

5

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to 10 the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in 15 water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

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EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

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A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that 30 recognize six-nucleotide restriction sites (MluI, MscI, Pvull, Sall and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the

subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most

recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in 5 prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low 10 expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 15 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to 20 previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350, 351 and 353-365.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels 25 in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

EXAMPLE 6
PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

5 6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100 μ g of P2S#12 and 120 μ g of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6 x 10⁶ cells/ml in complete media (RPMI-1640; Gibco 10 BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate 15 (Gibco BRL), non-essential amino acids (Gibco BRL), 2 x 10⁻⁵ M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed 20 (5mg/ml P2S#12 and 10mg/ml β 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 μ g/ml dextran sulfate and 25 μ g/ml LPS for 3 days). Six days later, cells (5 x 10⁵/ml) were restimulated with 2.5 x 10⁶/ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells 25 (Sherman et al, *Science* 258:815-818, 1992) and 3 x 10⁶/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x 10⁴ cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10⁵ cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in 30 Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice 5 were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 10 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on 15 the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2Kb were immunized as described 20 by Theobald *et al.* (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A^b binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6 x 10⁶ cells/ml in complete media (as described above) and cultured 25 in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells (5 x 10⁵/ml) were restimulated with 2.5 x 10⁶/ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3 x 10⁶/ml 30 A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2K_b tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown 5 in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2K_b targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

EXAMPLE 7

10 PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION
WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S. HLA A2K_b Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 µg P501S in the vector VR1012 either intramuscularly or intradermally. 15 The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2K_b-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at 20 least one naturally processed HLA-A2-restricted CTL epitope.

EXAMPLE 8

ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

25 This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8⁺ T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van 30 Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8⁺ T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a γ-interferon

ELISPOT assay (see Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 10^4 fibroblasts in the presence of 3 $\mu\text{g}/\text{ml}$ human β_2 -microglobulin and 1 $\mu\text{g}/\text{ml}$ P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, 5 fibroblasts transduced with HER-2/neu. Prior to the assay, the fibroblasts were treated with 10 ng/ml γ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts pulsed 10 with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/neu 15 gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

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EXAMPLE 9

ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL 25 response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the 30 addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8 $^+$ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts retrovirally transduced

to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (^{51}Cr release) and interferon-gamma production (Interferon-gamma Elispot; see above and Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

10

EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE-SPECIFIC ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100 μg of p5 peptide together with 140 μg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived

from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 ug/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of 5 the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

EXAMPLE 11

10 EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN
IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in 15 SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is provided in 20 SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly 25 expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).

EXAMPLE 12

30 GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND
STIMULATION TECHNIQUES WITH PROSTATE-SPECIFIC ANTIGEN

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- γ ELISPOT analysis as described above. Using a panel of 5 HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a 10 multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that 15 specifically produced interferon- γ when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- γ in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

20 To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened 25 in IFN-gamma ELISPOT assays against these A2Kb targets transduced with the "library" of P501S fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were 30 also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN-gamma assay. Only peptides

P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

5 In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8+ T cells were cultured with autologous CD40
10 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as
15 demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-
A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-
20 P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

EXAMPLE 13
IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS
BY MICROARRAY ANALYSIS

25

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in
30 prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOS:385-400. Of these sequences

SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

5

Table I
Summary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of 5 prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is 10 not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as 15 compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal 20 tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% 25 normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang 30 showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97%

of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

10

EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS
BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify
15 prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatzis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which

expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II
Prostate cDNA Libraries and ESTs

5

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups:

10 Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group

15 libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (*see* Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV
Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
439	22851	PAP

440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

EXAMPLE 15

FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

5

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened 10 using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-461 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences.

15

EXAMPLE 16

FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

20 This Example describes the full length cloning of P710P.
The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane

filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four
5 sequences were obtained, and are presented in SEQ ID NO: 468-471 These sequences appear to represent different splice variants of the P710P gene.

EXAMPLE 17

PROTEIN EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

10

This example describes the expression and purification of the prostate-specific antigen P501S in *E. coli*, baculovirus and mammalian cells.

a) Expression in *E. coli*

15 Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an
20 antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min,
25 and lastly by 1 cycle of 72°C for 10 min. The PCR product was cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was
30 induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A

(Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands were also observed, probably due to aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) was prepared as follows. P501S DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c) Expression of P501S in mammalian cells

Full-length P501S (553AA) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The Fugene/DNA mixture

was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 µl of GenePorter was diluted in 500 µl of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2 µg of plasmid DNA that was diluted in 500 µl of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

EXAMPLE 18

PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

20 a) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

25 A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using 30 ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to

generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were 5 generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

10 **Table V**
Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant (μg/ml)
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. 15 Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1 μg/ml, followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of 20 infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate

specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the 5 surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 10 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody 15 specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. 20 Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently 25 expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of 30 normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr.

HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach 5 was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and 10 subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with 15 HRP-conjugated donkey anti-mouse IgG (H+L)Affinipure F(ab') fragment (Jackson Immunoresearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array 20 immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM 25 citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

30 **b) Preparation and Characterization of Antibodies against P503S**

A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits

and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

5

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

The DNA sequences encoding the complementarity determining regions (CDRs) for 10 the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows. 15 The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells 20 and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further

15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception
5 of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

10 Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat
15 anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis
20 was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary,
25 pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal
30 antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the

appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

5 c) Preparation and Characterization of Antibodies against P703P

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal antibodies were isolated using SLAM technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptr1	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptr1	Rabbit monoclonal
8H2	P703Ptr1	Rabbit monoclonal
7H8	P703Ptr1	Rabbit monoclonal

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

25 The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk-/- cells either untransfected or transfected with a plasmid

expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

10 Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

15

EXAMPLE 19

CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen
20 P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that
25 following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains.
30 Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as

described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparagine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (i.e. intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM

sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by 5 SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma 10 membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter 15 plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with 20 phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates 25 were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

30 In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above.

To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server (<http://www-genome.wi.mit.edu/cgi-bin/contig/rhMapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al. Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

25

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

30

CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-10 315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536;

(b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and

15 (c) complements of any of the sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID No: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 20 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing 25 polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

4. An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a prostate-specific protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the protein 5 comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 10 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate-specific protein, or a 15 variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 20 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide comprising a sequence recited in any one 25 of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536.

7. An isolated polynucleotide comprising a sequence that hybridizes under moderately stringent conditions to a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111,
5 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-
225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390,
392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-
444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536.

10 8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector comprising a polynucleotide according to any one of claims 4-8.

15 10. A host cell transformed or transfected with an expression vector according to claim 9.

20 11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate-specific protein, the protein comprising an amino acid sequence encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-
25 160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225,
227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392,
393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444,
446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536 or a complement of any of the foregoing polynucleotide sequences.

30

12. A monoclonal antibody that specifically binds to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 519, 520, 522 and 539-551.

5 13. A monoclonal antibody comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

10 14. A fusion protein comprising at least one polypeptide according to
claim 1.

15 15. A fusion protein according to claim 14, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

16. A fusion protein according to claim 14, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

20 17. A fusion protein according to claim 14, wherein the fusion protein comprises an affinity tag.

18. An isolated polynucleotide encoding a fusion protein according to
claim 14.

25 19.. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to any one of claims 11-13;
- 30 (d) a fusion protein according to claim 14; and

(e) a polynucleotide according to claim 18.

20. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- 5 (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to any one of claims 11-13;
- (d) a fusion protein according to claim 14; and
- (e) a polynucleotide according to claim 18.

10

21. A vaccine according to claim 20, wherein the immunostimulant is an adjuvant.

22. A vaccine according to claim 20, wherein the immunostimulant 15 induces a predominantly Type I response.

23. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 19.

20

24. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

25. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

26. A pharmaceutical composition according to claim 25, wherein the antigen presenting cell is a dendritic cell or a macrophage.

27. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.

5 28. A vaccine according to claim 27, wherein the immunostimulant is an adjuvant.

29. A vaccine according to claim 27, wherein the immunostimulant induces a predominantly Type I response.

10

30. A vaccine according to claim 27, wherein the antigen-presenting cell is a dendritic cell.

31. A method for inhibiting the development of a cancer in a patient, 15 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, and thereby inhibiting the development of a cancer in the patient.

20

32. A method according to claim 31, wherein the antigen-presenting cell is a dendritic cell.

33. A method according to any one of claims 23, 24 and 31, wherein the 25 cancer is prostate cancer.

34. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the protein comprises an amino acid sequence that is 30 encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

5 wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate-specific protein from the sample.

35. A method according to claim 34, wherein the biological sample is
10 blood or a fraction thereof.

36. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

15 37. A method for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;

20 (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); and

(iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii),

25 under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

38. An isolated T cell population, comprising T cells prepared according to the method of claim 37.

39. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 38.

5 40. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:

10 (i) a polypeptide according to claim 1;

(ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

15 (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

20

41. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:

25 (i) a polypeptide according to claim 1;

(ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

30 (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

5 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

42. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

10 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

15 (i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

20 (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

(c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

43. A method according to claim 42, wherein the binding agent is an antibody.

25

44. A method according to claim 43, wherein the antibody is a monoclonal antibody.

45. A method according to claim 42, wherein the cancer is prostate 30 cancer.

46. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;
- 10 (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- 15 (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

47. A method according to claim 46, wherein the binding agent is an antibody.

20

48. A method according to claim 47, wherein the antibody is a monoclonal antibody.

25 49. A method according to claim 46, wherein the cancer is a prostate cancer.

50. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein,

wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

5 (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

10

51. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15

52. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

20

53. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

5 54. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

10 55. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

15 56. A diagnostic kit, comprising:
(a) one or more antibodies according to claim 11; and
(b) a detection reagent comprising a reporter group.

57. A kit according to claim 56, wherein the antibodies are immobilized on a solid support.

20 58. A kit according to claim 56, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

25 59. A kit according to claim 56, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

30 60. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45,

47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171,
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5 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any
of the foregoing polynucleotides.

61. A oligonucleotide according to claim 60, wherein the
oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO:
10 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-
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442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536.

15

62. A diagnostic kit, comprising:
(a) an oligonucleotide according to claim 61; and
(b) a diagnostic reagent for use in a polymerase chain reaction or
hybridization assay.

20

63. A host cell according to claim 10, wherein the cell is selected from
the group consisting of: *E. coli*, baculovirus and mammalian cells.

64. A recombinant protein produced by a host cell according to claim
25 10.

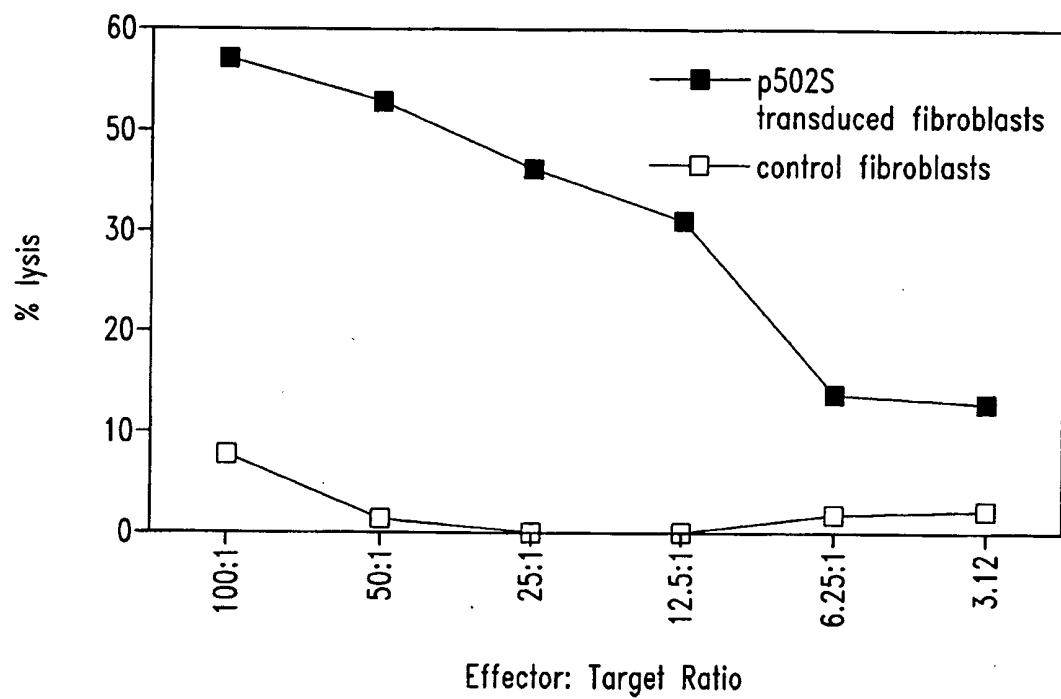


Fig. 1

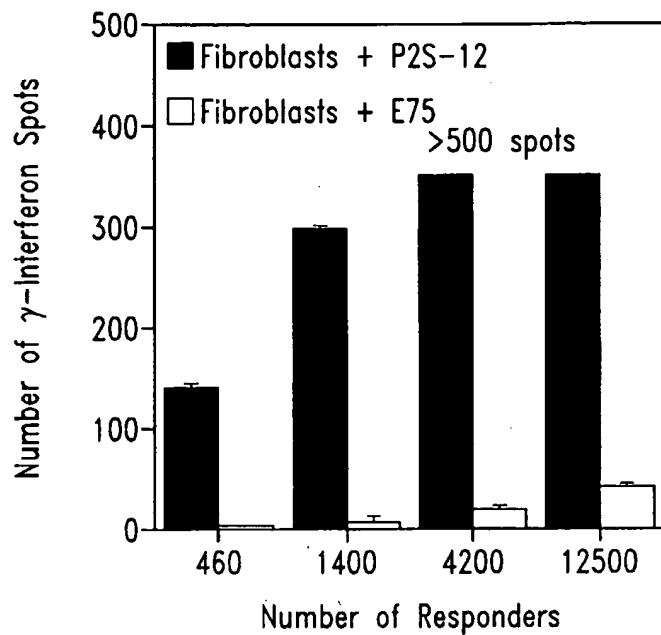


Fig. 2A

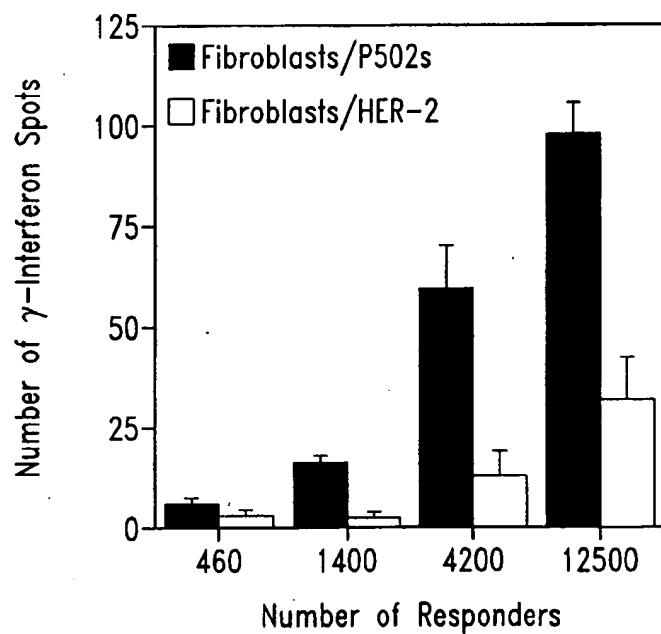


Fig. 2B

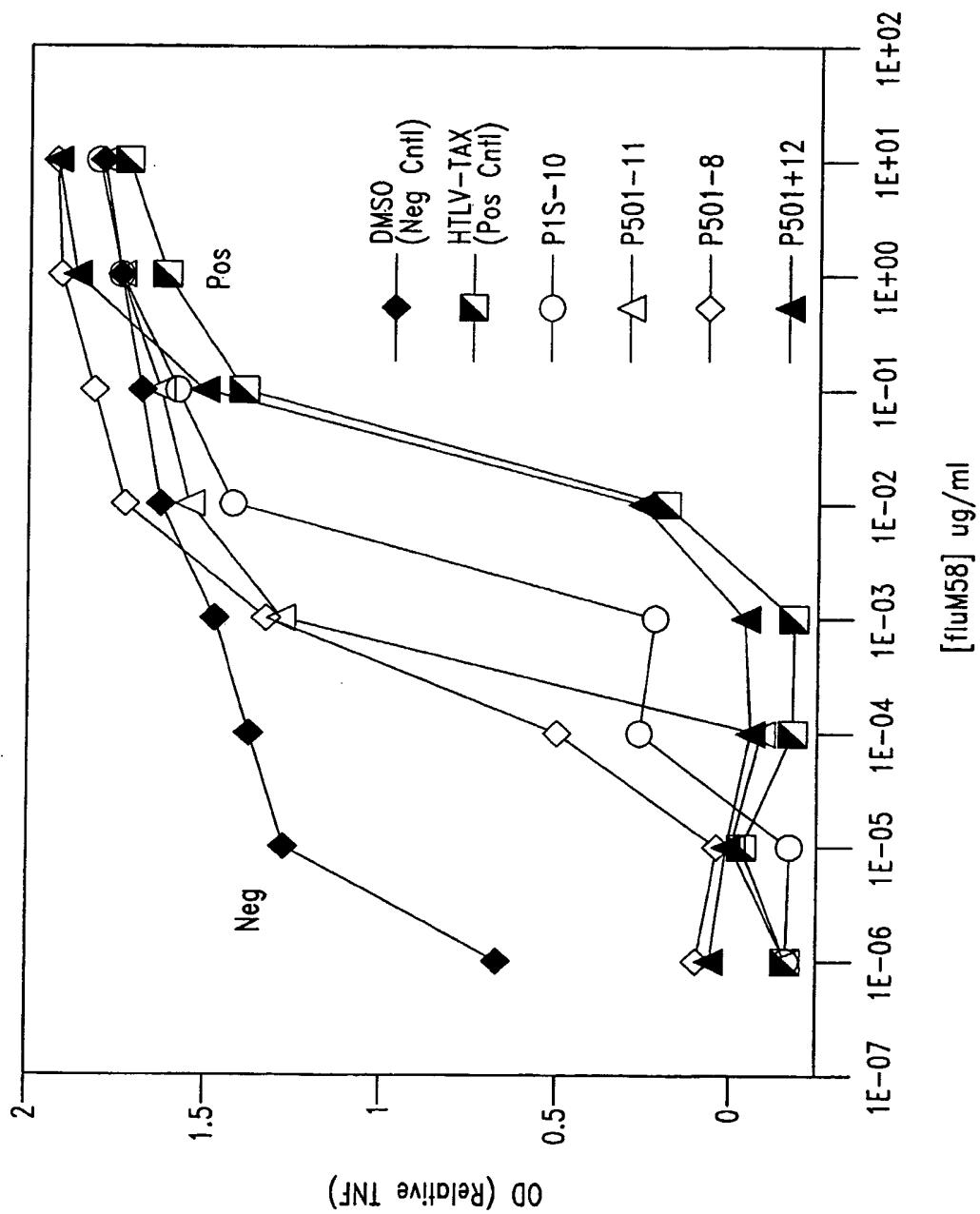


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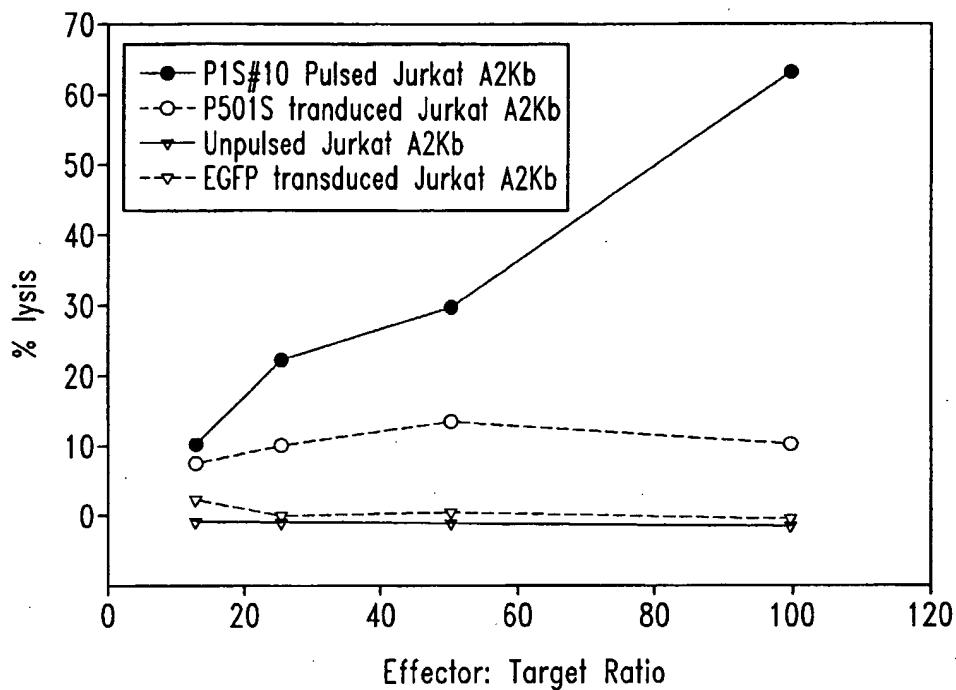


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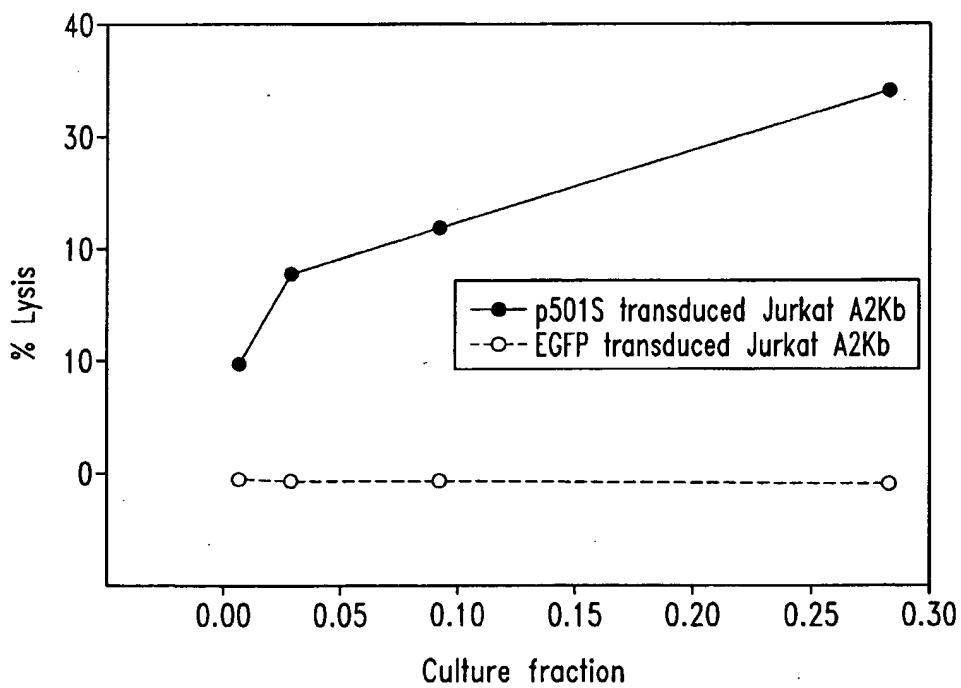


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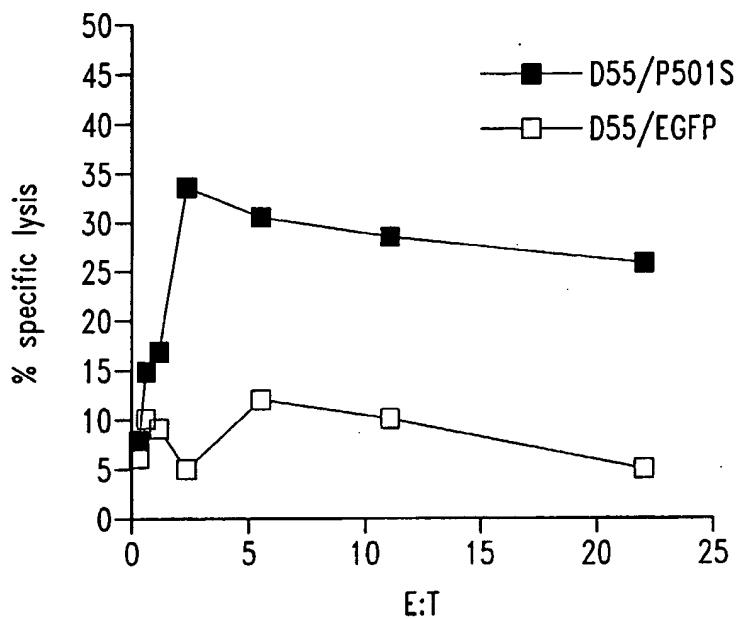


Fig. 6A

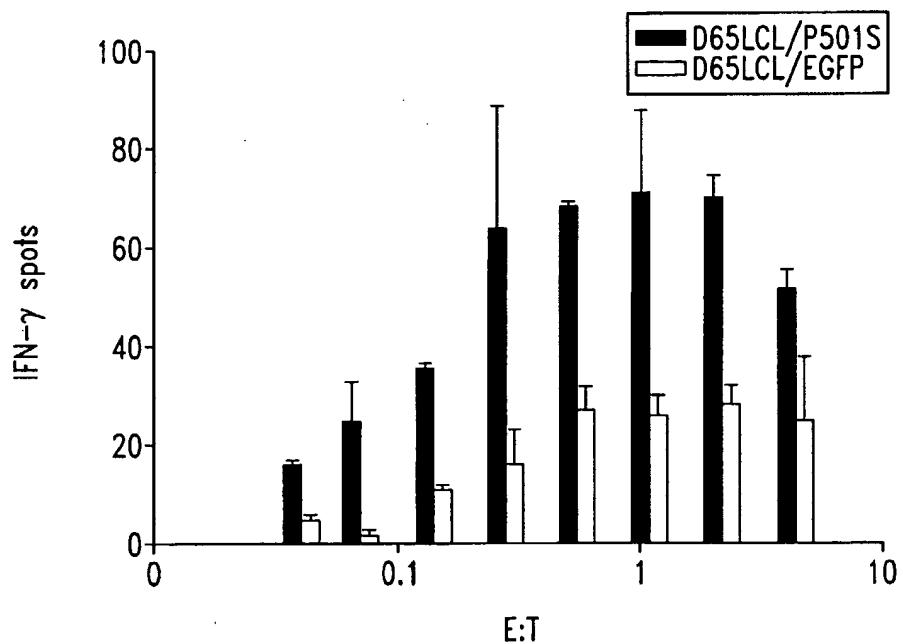
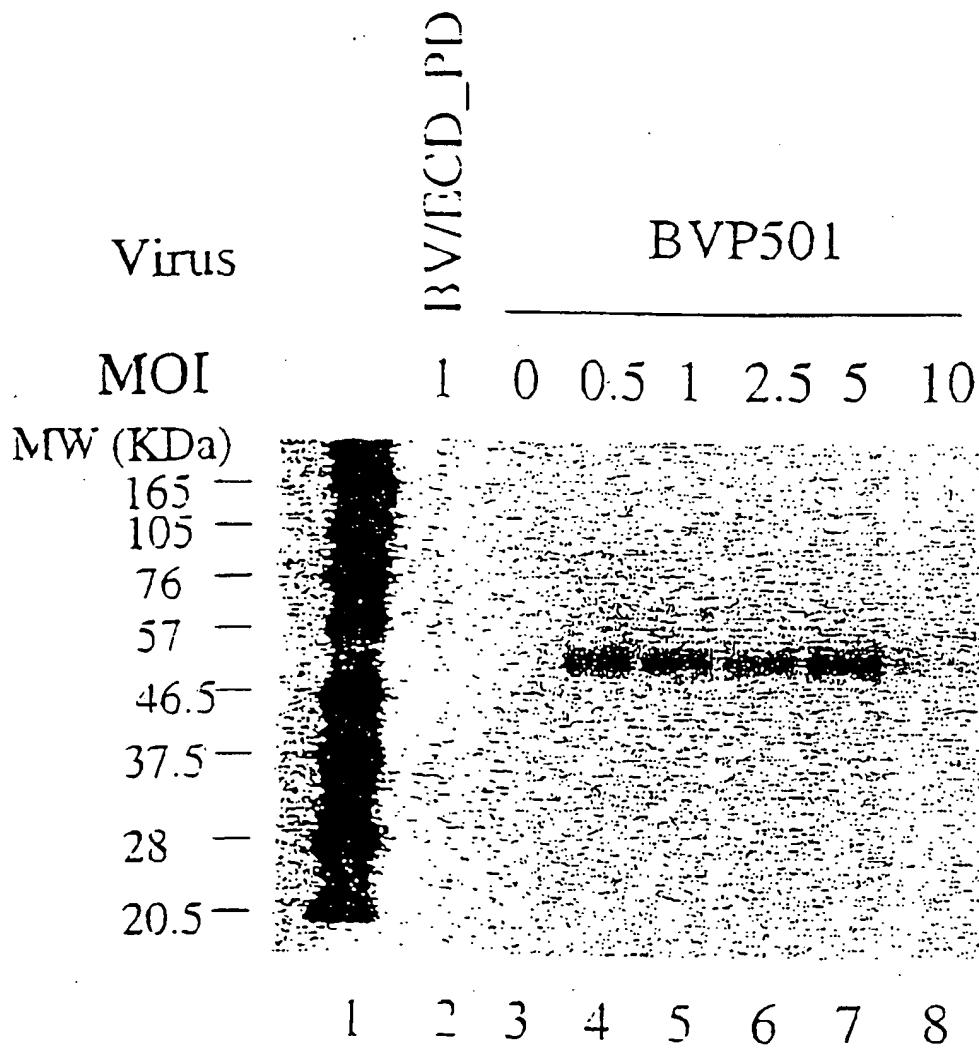


Fig. 6B

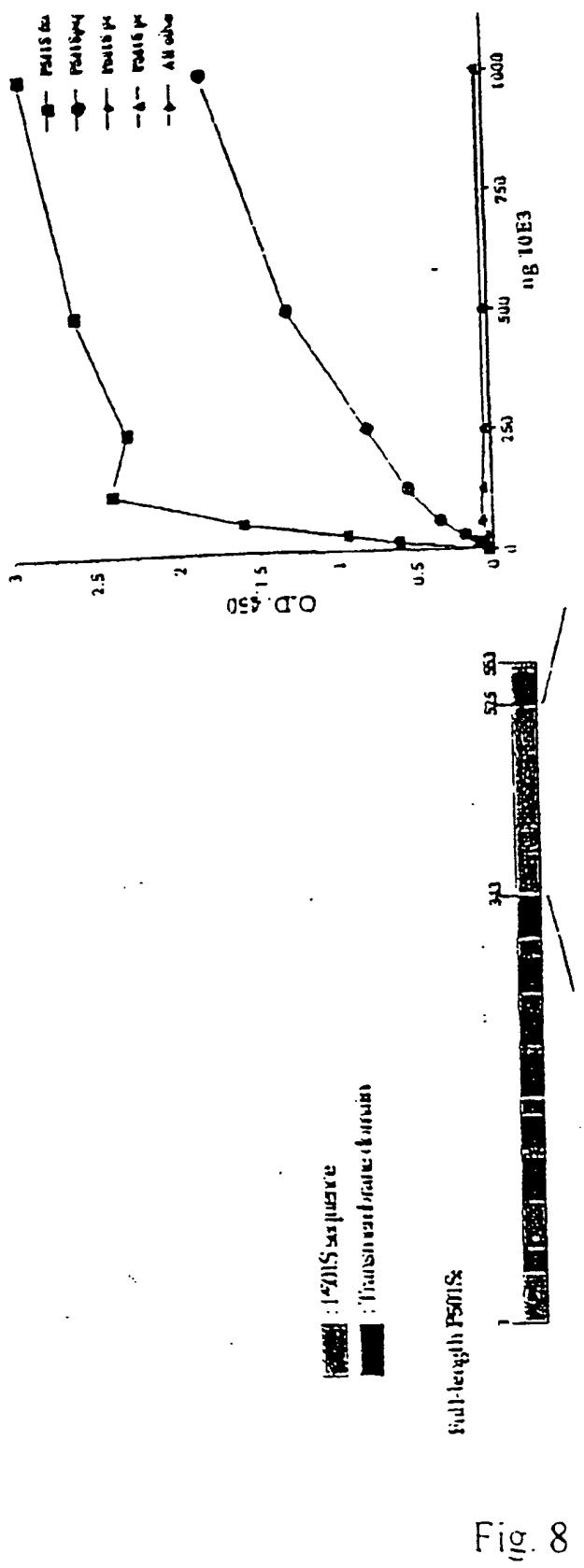
Expression of P501S
by the Baculovirus Expression System



0.6 million high 5 cells in 8-well plate were infected with an unrelated control virus BV/ECD_PD (lane 1), without virus (lane 3), or with recombinant baculovirus for P501 at different MOIs (lane 4 - 8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (Sigma).

Fig. 7

Figure 8. Mapping of the epitope recognized by 10E3-G4-D3



PSIS fragment used for immunization:

三

/10

Schematic of P501S with predicted
transmembrane, cytoplasmic, and extracellular regions

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TMVLGIGPVVLGVCPPLLGSAS

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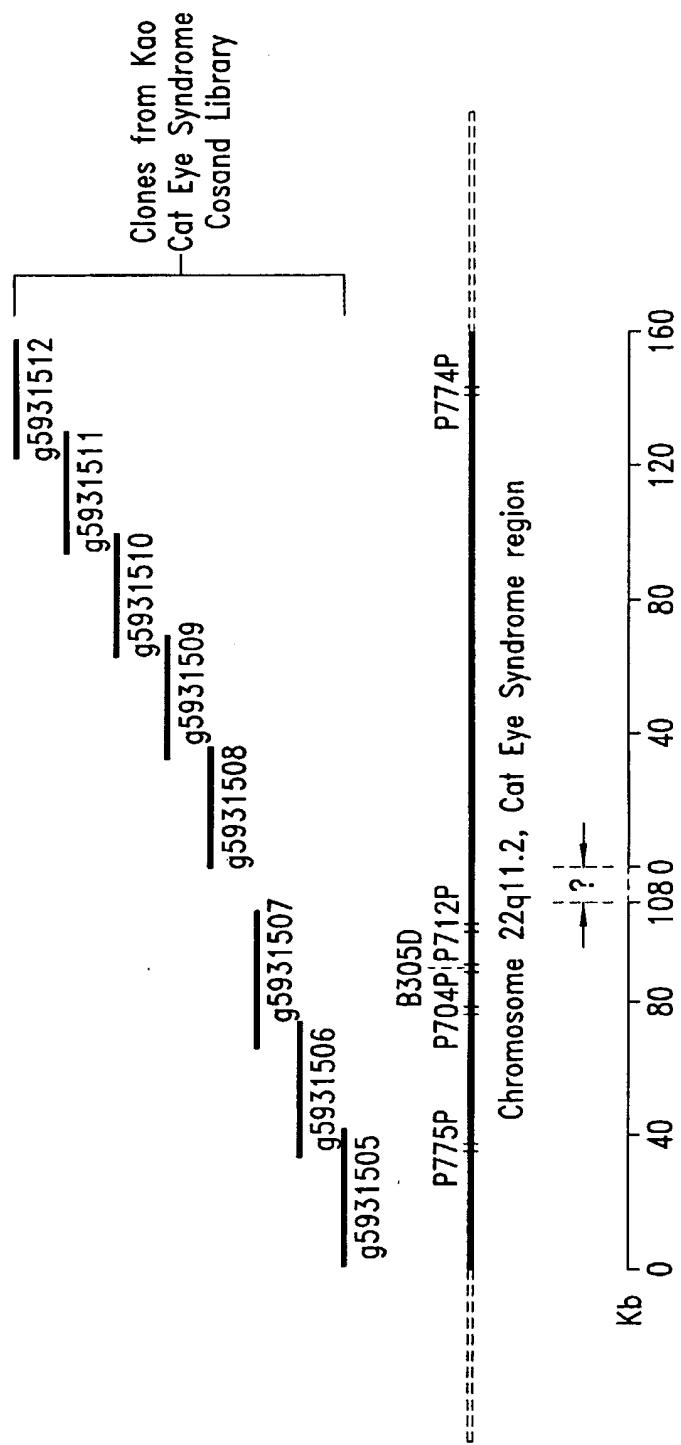
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VTAYMVSAGLGLVAIYFAT QVVFDFKSDLAKYSA

Underlined sequence: Predicted transmembrane domain; **Bold sequence**:
 Predicted extracellular domain; *Italic sequence*: Predicted intracellular
 domain. Sequence in bold/underlined: used generate polyclonal rabbit
 serum

Localization of domains predicted using HMMTOP (G.E. Tusnady an I. Simon
 (1998) Principles Governing Amino Acid Composition of Integral Membrane
 Proteins: Applications to topology Prediction. J.Mol Biol. 283, 489-506.

Fig. 9

*Fig. 10*

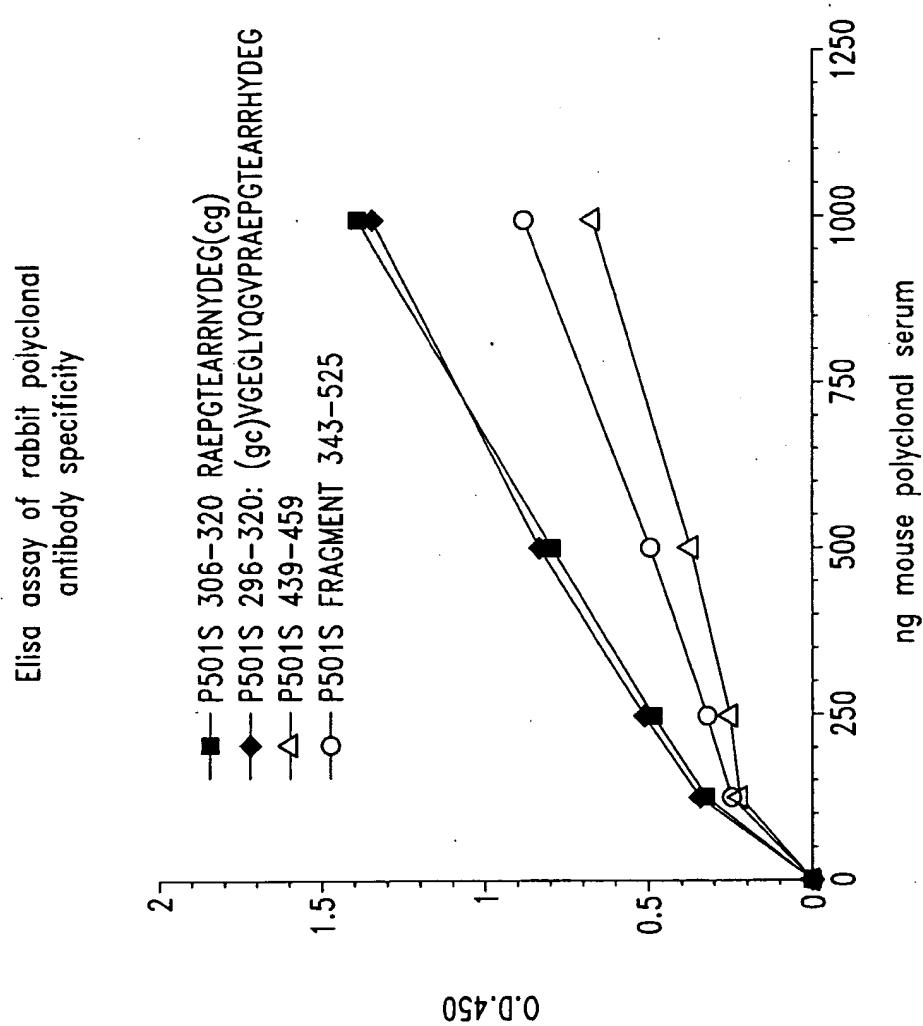


Fig. 11

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Reed, Steven G.
Kalos, Michael
Fanger, Gary
Retter, Mark
Solk, John
Day, Craig
Skeiky, Yasir A.W.
Wang, Aijun

<120> COMPOSITIONS AND METHODS FOR THE THERAPY AND
DIAGNOSIS OF PROSTATE CANCER

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ctgaagcgca	cgtccccagaa	ggtggaacttg	gcaactgaaac	agctgggaca	catcccgcgag	180
taclgaacacgc	gcctgaaagt	gctggagcgg	gaggtccagc	agtgtagccg	cgtcctgggg	240
tgggtggccg	angcctganc	cgctctgcct	tgtgtcccccc	angtgggccc	ccaccccccctg	300
acctgcctgg	gtccaaacac	tgagccctgc	tggcggactt	caagganaac	ccccacangg	360
ggattttgt	cctanantaa	ggctcatctg	ggcctcgcc	cccccacctg	gttggccttg	420
tctttgangt	gagcccccatt	tccatctggg	ccactgtcng	gaccacctt	ngggagtgtt	480
ctccttacaa	ccacannatg	cccggtctct	cccgaaaaacc	antcccanc	tgngaaggat	540
caagnctgn	atccactnnt	nctanaaccg	gcenccnccg	cngtggaaacc	cnccctntgt	600
tccttttcnt	tnagggttaa	tnncgccttg	gccttnccan	ngtcctncnc	ntttccnnnt	660

gttnaaattg ttangcnccc nccnntccn cnncnnncnan cccgaccnn annnnann	720
ncctgggggt ncnnncngat tgacccncc nccctntant tgcntnggg nncnntgccc	780
cttccctct ngganncg	799
<210> 9	
<211> 801	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(801)	
<223> n = A,T,C or G	
<400> 9	
acgccttgat cttccccaggc tgggactggc tctgggagga gcccggcatg ctgtggtttgc	60
taangatgac actccccaaag gtggtcctga cagtggccca gatggacatg gggctcacct	120
caaggacaag gccaccaggc gcggggggccg aagcccatat gatccttact ctatgagcaa	180
aatccctgt gggggcttct cttgaagtc cggccancagg gtcagtctt tggacccang	240
caggtcatgg gttgtngnc caactggggc ccncaacgca aaangcnca gggcctcngn	300
caccatccc angacgcggc tacactnctg gacccctccncc tccaccactt tcatgegctg	360
ttcntacccg cgnatntgtc ccanctgtt cngtccnac tccancttct nggacgtgcg	420
ctacatacgc cccgantcncc ntcccgctt tgccttccatc cacgtncan caacaaattt	480
cnccntantg cacnattcc acnnttncn agntttccncc nnccngcttc ttntaaaag	540
ggtganccc cgaaaaatnc cccaaagggg gggggccnngg taccactn cccctnata	600
gctgaantcc ccatnaccnn gnctcnatgg anccntccnt tttaaannacn ttctnaactt	660
ggaanancc ctcgnccntr cccccnttaa tcccncccttgc cnangnnnt ccccnntcc	720
nccnnntng gcntntnann cnaaaaaggc ccnnnnancaa tctcctnnccn ctcanttcg	780
ccancctcg aaatcgcccn c	801
<210> 10	
<211> 789	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(789)	
<223> n = A,T,C or G	
<400> 10	
cagtctatnt gcccagtgtg gcagcttcc ctgtggctgc cgggccaca tgcctgtccc	60
acagtgtggc cttgggtgaca gcttcagccg ccctcacccgg gttcaccccttc tcagccctgc	120
agatccgtcc ctacacactg gcctccctt accaccggga gaagcaggtg ttcctgcccc	180
aataccgagg ggacactgtt ggtgcttagca gtgaggacag cctgtatgacc agcttccctgc	240
caggccctaa gcttggagct ccctcccta atggacacgt ggggtctggc ggcagtggcc	300
tgcctccacc tccaccccgcc ctctggggg cctctgcctg tgatgtctcc gtacgtgtgg	360
tggtgggtga gcccacccgan gccagggtgg ttccggggccg gggcatctgc ctggacccctg	420
ccatccgttga tagtgccttcc tgctgtccca ngtggcccca tccctgttta tgggctccat	480
tgtccagtc agccagtctg tcactgccta tatgggtgtc gcccaggcc tgggtctgg	540
cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagcg	600
ttaaaaaatt ccagcaacat tgggggtggc aggccctgcct cactgggtcc aactccccgc	660
tcctgttaac cccatggggc tgccggcttgc gcccaccaatt tctgtgtctg ccaaantnat	720
gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct nggggggtn	780
gngttccc	789
<210> 11	
<211> 772	

<212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(772)
 <223> n = A,T,C or G

<400> 11

cccacccctac	ccaaatatta	gacaccaaca	cagaaaagct	agcaatggat	tcccttctac	60
tttgttaaat	aaataagtta	aatatttaaa	tgcctgtgtc	tctgtatgg	caacagaagg	120
accaacaggc	cacatcctga	taaaaggtaa	gaggggggtg	gatcagcaaa	aagacagtgc	180
tgtgggctga	ggggacctgg	ttcttggtg	ttgcccctca	ggactcttcc	cctacaaaata	240
actttcatat	gttcaaatcc	catggaggag	tgtttcatcc	tagaaactcc	catgcaagag	300
ctacattaaa	cgaagctgca	ggttaagggg	cttanagatg	ggaaaccagg	tgactgagtt	360
tattcagctc	ccaaaaaccc	ttctctaggt	gtgtctcaac	taggaggcta	gctgttaacc	420
ctgagcctgg	gtaatccacc	tgcagagtcc	ccgcattcca	gtgcatggaa	cccttctggc	480
ctcccctgtat	aagtccagac	tgaaaccccc	ttggaaggnc	tccagtcagg	cagccctana	540
aactgggaa	aaaagaaaaag	gacgccccan	cccccagctg	tgcancctacg	cacctaaca	600
gcacagggtg	gcagaaaaaa	aaccacttta	cttggcaca	aacaaaaact	ngggggggca	660
accccgccac	ccnangggg	gttaacagga	ancngggnaa	cntggAACCC	aattnaggca	720
ggcccnccac	cccnaatntt	gctggaaat	tttcctccc	ctaaattntt	tc	772

<210> 12
 <211> 751
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(751)
 <223> n = A,T,C or G

<400> 12

gcccccaattc	cagctgccac	accaccacg	gtgactgcat	tagtcggat	gtcataaaaa	60
agctgattga	agcaaccctc	ta c ttttgg	tctgagcct	tttgc t ttgt	gcagg t ttca	120
ttggctgtgt	tggtacgtt	gtcattgca	cagaatgggg	gaaaggcact	gttcttttgc	180
aagtanggtg	agtccctaaa	atccgtatag	tttgtgaagc	cacagcactt	gagcccttcc	240
atgggttgtt	tccacacttg	agtgaagtct	tcctggaaac	cataatctt	tttgatggca	300
ggcactacca	gcaacgtcag	ggaagtgtc	agccattgtg	gtgtacacca	aggcgaccac	360
agcagctgcn	acctcagcaa	tgaagatgan	gaggangatg	aagaagaacg	tcncgagggc	420
acacttgc	tcagtttan	caccatanca	gcccntgaaa	accaananca	aagaccacna	480
cnccggctgc	gatgaagaaa	tnacccncg	ttgacaaaact	tgcacggc	tggganccac	540
agtggcccn	aaaatctca	aaaaggatgc	cccatcnatt	gacccccc	atgcccactg	600
ccaacagggg	ctgccccacn	cncnnnaacga	tgancnnatt	gnacaagatc	tncntggct	660
tnatnaacnt	gaaccctgcn	tntgtgctcc	tgttcaggnc	cnnggcctga	cttctnaann	720
aangaactcn	gaagnccca	cnnganann	g			751

<210> 13
 <211> 729
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(729)
 <223> n = A,T,C or G

<400> 13

gagccaggcg tccctctgcc	tgcccactca	gtggcaacac	ccgggagctg	ttttgtcctt	60
tgtggancct cagcagtnc	ctcttcaga	actcantgcc	aagancctg	aacaggagcc	120
accatgcagt gcttcagctt	cattaagacc	atgatgatcc	tcttcaattt	gctcatctt	180
ctgtgtggtg cagccctgtt	ggcagtgggc	atctgggtgt	caatcgatgg	ggcatcctt	240
ctgaagatct tcgggcaact	gtcgccagt	gccatgcagt	ttgtcaacgt	gggctacttc	300
ctcatcgccag cccgcgttgt	ggtcttagct	ctaggtttcc	tgggctgcta	tggtgctaag	360
actgagagca agtgtgccc	cgtgacgttc	ttcttcatcc	tcctcctcat	tttcattgct	420
gaggttgc当地	tgctgtggtc	gccttgggt	acaccacaat	ggctgagcac	480
tgctggtaat gcctgccatc	aanaaaaat	tatgggttcc	caggaanact	tcactcaagt	540
gttggAACAC	caccatgaaa	gggctcaagt	gtctggctt	cnncacaacta	600
gaagantcac ctacttcaaa	gaaaanagt	ccttcccccc	atttctgtt	caattgacaa	660
acgtccccaa cacagccaat	tgaaaacctg	cacccaaccc	aaanggtcc	ccaaccanaa	720
attnaaggg					729

<210> 14

<211> 816

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(816)

<223> n = A,T,C or G

<400> 14

tgctctcct caaagttgtt	cttgttgc当地	taacaaccac	cataggtaaa	gcggggcgca	60
tgttcgtga aggggtgtt	gtaccagcgc	gggatgctct	ccttgc当地	tcctgtgtct	120
ggcaggtcca cgc当地	tttgc当地	gggaaatgga	tgc当地	ctcgctaaag	180
ccactcgctt attttcaca	ggcagcctcg	tccgacgcgt	cgggcagtt	gggggtgtct	240
tcacactcca gggaaactgtc	natgc当地	ccattgctgc	agc当地	ggtgggctga	300
cangtgc当地	agcacactgg	atggc当地	tccatgnnan	gggc当地	360
tgancccc当地	anctgc当地	caaangcccc	accttgcaca	ccccgacagg	420
atcttctcc	c当地	ttnttctt	tgcccaancc	anccc当地	480
gcanatctgc tccgnggggg	tc当地	antantacc	ancgtggaa	aagaacccca	540
caancttgc当地	tggatn	gca	nataatct	ncnttctgc	600
ctgtnnanct ttagncn	gtc当地	cttgg	nnctt	aacctaatcn	660
gggacaagg	ta	ntngccn	c当地	ccnnntcaact	720
cncnctct	ccc当地	ttt当地	ccnancn	ccccctgg	780
cacaaccctn	cccc	cccc	cccc	ttt	816

<210> 15

<211> 783

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(783)

<223> n = A,T,C or G

<400> 15

ccaaggcctg ggc当地	nacttgaagg	tacaacccca	ggaacccctg	gtgctgaagg	60
atgtggaaaa	cacagattgg	cgc当地	ggggtgacac	ggatgtcagg	120
aagacccaaa	ccaggtggaa	ctgtggggac	tcaaggaaang	cacctacctg	180
cagtgactag	ctc当地	ccagaggaca	cggccaacgt	cacagtca	240
ccaaggcagac	agaagactac	tgc当地	ccaacaangt	gggtcgctgc	300
tcccacgctg	gtactatgac	ccc当地	gagatctgaa	ggggctt	360

gcttggcaa	caagaacaac	taccttcggg	aagaagagtg	cattctancc	tgtcnnggtg	420
tgcaagggtgg	gcctttgana	ngcanctctg	gggctcangc	gactttcccc	cagggcccct	480
ccatggaaag	gcccaccca	ntgttctctg	gcacctgtca	gcccacccag	ttccgctgca	540
ncaatggctg	ctgcatcnac	antttctng	aatttgtgaca	acacccccc	ntgcccccaa	600
ccctcccaac	aaagcttccc	tgttnaaaaa	tacnccant	ggctttnac	aaacncccg	660
cncctccntt	ttccccnnntn	aacaaaggc	nctngcnntt	gaactgccc	aaccnngaa	720
tctnccnngg	aaaaantncc	ccccctggtt	cctnnaanc	cctccncnaa	anctncccc	780
ccc						783

<210> 16
<211> 801
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G

<400> 16						
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agctgattga	agcaaccctc	tacttttgg	tcgtgacgc	tttgcttgg	gcaggttca	120
ttggctgtgt	tggtaacgtt	gtcattgca	cagaatgggg	gaaaggcact	tttcttttgc	180
aagttaggggt	agtccctaaa	atccgtatag	tttgtaaggc	cacagcactt	gagccctttc	240
atggtgtgt	tccacacttg	agtgaagtct	tcctgggaac	cataatcttt	cttgcattggca	300
ggcactacca	gcaacgtcag	gaagtgcac	gccattgtgg	tgtacaccaa	ggcgaccaca	360
gcagctgca	cctcagcaat	gaagatgagg	aggaggatga	agaagaacgt	cncgaggggca	420
cacttgcct	ccgtcttagc	accatagcag	ccangaaac	caagagcaaa	gaccacaacg	480
ccongctgca	atgaaagaaa	ntacccacgt	tgacaaactg	catggccact	ggacgacagt	540
tggcccgaa	atcttcagaa	aaggatgcc	ccatcgattt	aacaccana	tgcccactgc	600
cnacagggt	gcncncncn	gaaagaatga	gccattgaag	aaggatcntc	ntggtcttaa	660
tgaactgaaa	ccntgcatgg	tggccctgt	tcagggctct	tggcagtgaa	ttctganaaa	720
aaggaacngc	tnagcccc	ccaaangana	aaacacccc	gggtgttgcc	ctgaattggc	780
ggccaaggan	ccctgccccn	g				801

<210> 17
<211> 740
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(740)
<223> n = A,T,C or G

<400> 17						
gtgagagcca	ggcgccctc	tgcctgccc	ctcagtggca	acacccggga	gctgtttgt	60
cctttgtgga	gcctcagcag	ttccctctt	cagaactcac	tgccaaagac	cctgaacagg	120
agccaccatg	cagtgttca	gcttcattaa	gaccatgatg	atcctcttca	atttgcctat	180
ctttctgtgt	ggtgcagccc	tgttggcagt	ggcatctgg	gtgtcaatcg	atggggcattc	240
ctttctgaag	atcttcgggc	cactgtcg	cagtgcac	cagttgtca	acgtggctca	300
cttccatc	gcagccggcg	ttgtggctt	tgctcttgg	ttccctggct	gtatggtgc	360
taagacggag	agcaagtgt	ccctcgat	gttcttctt	atcctccctcc	tcatcttcat	420
tgctgaagtt	gcagctgt	tggtcgcctt	ggtgtacacc	acaatggctg	aaccattcc	480
gacgttgctg	gtantgcctg	ccatcaanaa	agattatggg	tcccaaggaa	aaattcactc	540
aannttgaa	cacnccatg	aaaagggctc	caatttctgn	tggcttcccc	aactataccg	600
gaattttgaa	agantnccc	tacttccaaa	aaaaaanant	tgcctttncc	ccnntctgt	660
tgcaatgaaa	acntccaa	acngccaaatn	aaaacctgcc	cnncaaaaa	ggntcncaaa	720

caaaaaaaant nnaagggttn	740
<210> 18	
<211> 802	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(802)	
<223> n = A,T,C or G	
<400> 18	
ccgctggttg cgctggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca	60
caaggcttc cagctgccgc acattacgca gggcaagagc ctccagcaac actgcataatg	120
ggatacactt tacttttagca gccagggta caactgagag gtgtogaagc ttattcttct	180
gagcctctgt tagtggagga agattccggg cttcagctaa gtatcagcg tatgtcccat	240
aagcaaacac tttgagcagc cggaaaggtag aggcaaagtc actctcagcc agctctctaa	300
cattgggcat gtccagcagt tctccaaaca cgttagacacc agnggctcc agcacctgtat	360
ggatgagtgt gcccagcgct gcccccttgg ccgacttggc taggagcaga aattgctct	420
ggttctgccc tttcacccttc acttccgcac tcatcactgc actgagtggt ggggacttgg	480
gttcaggatg tccagagacg tggttccgcc ccctcnctta atgacaccgn ccanncacc	540
gtcggcteccc gccgantngt ttctgtccttcc ctgggtcagg gtctgtggc cnctacttgc	600
aanccttcgtc nggcccatgg aattcaccnc accggaactn gtangatcca ctnnttctat	660
aaccggncgc caccgcnnnt ggaactccac tcttnnncc ttacttgag gtttaaggtc	720
acccttnncg ttaccttggt ccaaaccntn cctgtgtcg anatngtnaa tcnggnccna	780
tnccanccnc atangaagcc ng	802
<210> 19	
<211> 731	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(731)	
<223> n = A,T,C or G	
<400> 19	
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gagcccaccc tcacngggng gngtctttat nggagggggc ggagccacat cnctggacnt	120
cntgacccttca actccccncc ncncantgca gtatcactgtc cagaactgaa ggtacgtgg	180
caggaaccaa gancaaannc tgctccnncc caagtcggcn naggggcgg ggctggccac	240
gcncatccnt cnagtjctgn aaagccccnn cctgtctact tgtttgaga acngcnngn	300
catgcccagn gttanataac nggcngagag tnannttgc tctcccttcc ggctgcgcac	360
cngntntgct tagnggacat aacctgacta cttaaactgaa cccnngaatc tnccnccct	420
ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcactgtc tgctcaagta	480
aagtgtaccc catncccaat gtntgctngt ngctctgncc tgcnttangt tcggctctgg	540
gaagacatat caattnaagc tatgtttctg actgccttctt gtccttgna acaancnacc	600
cnnccnntcc aaaaaaaaaaaaaaaaat ccccccaccc ntnaattnan ttancccn	660
cccccnngcc cggcctttta cnancntcnn nnacngggna aaaccnnngc tttncccaac	720
nnaatccncc t	731
<210> 20	
<211> 754	
<212> DNA	
<213> Homo sapien	

<220>
 <221> misc_feature
 <222> (1)...(754)
 <223> n = A,T,C or G

<400> 20

tttttttttt tttttttttt taaaaacccc	ctccattnaa tgnaaacttc	cgaaattgtc	60
caacccctc ntccaaatnn ccnttccgg	gnngggggttc	caaacccaan ttanntttgg	120
annttaaatt aaatnttnnt	tggnggnnna	ancnaatgt nangaaagtt naacccanta	180
tnancttnaa tnccctggaaa	ccngtngntt	ccaaaaaatntt ttaaccctta antccctcg	240
aaatngttta ngaaaaaccc	aanttcnt	aagggttgttt gaaggntnaa tnaaaanccc	300
nnccaattgt ttttngccac	gcctgaatta attggnttcc	gntgtttcc nttaaaanaaa	360
ggnnanccccc ggtantnaa	tcccccnnc	cccaattata ccgantttt ttngaattgg	420
ganccncgg gaattaacgg	ggnnnnntccc	tnttgggggg cnggnncccc cccntcg	480
ggttngggnc aggnccnaat	tgttaaggg	tccgaaaaat ccctccnaga aaaaaanctc	540
ccaggntgag nntngggttt	nccccc	cangggccct ctegnanagt tggggtttgg	600
ggggcctggg atttnttcc	ccctnttncc	tccccccccc ccnggganag aggttngngt	660
tttgntcnnc gcccccnccn	aagancttn	ccganttnan ttaaatccnt gcctnggcga	720
agtccnttgn aggntaaan	ggccccctnn	cggg	754

<210> 21
 <211> 755
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(755)
 <223> n = A,T,C or G

<400> 21

atcancat gaccccnaac nnggaccnc	tcancggnc nnnnacnc	cggccnatca	60
nngtnagnnc actncnntn	natcacnc	cnccnactac gcccncnanc	120
nncanatncc actganngcg	cgangtngan	ngagaaanct nataccanag ncacccanacn	180
ccagctgtcc nanaangcct	nnnataengg	nnnatccaat ntgnancctc	240
nnccnccanat gatttctn	anccgattac	ccntnccccc tanccctcc	300
cgaaggcnct ggnccnaagg	nngcgncc	ccgctagntc cccnncaagt cncncnccta	360
aactcanccn nattacncgc	ttcnttagta	tcaactcccg aatctcaccc tactcaactc	420
aaaaanatcn gataaaaaat	aatncaagcc	tgnttatnac actntgactg	480
ttagnggtcc ntnaancntc	ctaatacttc	ggtctctatt cagtcnct tcnccaattt	540
ctttcngaca gcatntttt	gttccnnntt	ccnaanggct gggttcttan	600
gggctcnctct tttccttcgg	ttancctgg	ttcnccggc cagttattat	660
aaattcntnc cnttnttt	tggcnttcna	aaccccccggc cttgaaaacg	720
aaaaggttgt tttganaaaa	tttttgg	gccccccgg	755

<210> 22
 <211> 849
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(849)
 <223> n = A,T,C or G

<400> 22

ttttttttt tttttangtg	tngtcgtgca	ggttagaggct tactacaant	gtgaanacgt	60
acgctnggan taangcgacc	cganttctag	gannccctt	aaaatcanac tgtgaagatn	120

atcctgnnna	cggaanggtc	accggnnat	nntgctaggg	tgnccnctcc	cannncnttn	180
cataactcng	ngccctgcc	caccaccc	ggcgcccng	ngncgggccc	cgggtcattn	240
gnnttaaccn	cactnngcha	ncggttccn	nccccnnccn	acccnngcga	tccggggtncc	300
tctgtttcc	cctgnagnch	anaaaantggg	ccncggnccc	ctttaaaaa	nnacaaggca	360
cngccnctca	nccnengccc	ccccccant	nngggggact	gccnanngct	cgfttnctng	420
nnaccnnnn	ggtnccctcg	gttgtcgant	cnacccgnang	ccanggattc	cnaaggaaagg	480
tgcgttnttgc	gcccctaccc	ttcgctncgg	nncacccttc	ccgacnanga	nccgctcccg	540
cncnnngng	cctcneetcg	caacacccgc	nctentcngr	ncggnnnnccc	ccccacccgc	600
nccctcnnc	ngncgnancn	ctccnncc	gttcannca	ccaccccgcc	ccgcccaggcc	660
ntcancacn	ggngacnng	nagcnccnntc	gcnccgcn	gcnccnccct	cgccncngaa	720
ctnctnctng	ccantnnncgc	tcaanccnna	chaaacgccc	ctgcgcggcc	cgnagegncc	780
ncctccnccg	gtcctcccg	cttccnaccc	angnnttccn	cgaggacacn	nnaccncggc	840
nncangcgg						849

<210> 23
<211> 872
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(872)
<223> n = A,T,C or G

<400> 23

gchgcaacta	tacttcgctc	gnactcggtc	gcctcgctnc	tcttttcctc	cgcaaccatg	60
tctgacnanc	ccgattinggc	ngatatcnan	aagntcganc	agtccaaact	gantaacaca	120
cacacnccn	aganaaatcc	nctgccttc	anagtnaan	attgaacnng	agaaccangc	180
nggcgaatcg	taatnaggcg	tgcgcgc	atntgtcncc	gtttattnntn	ccagcntcnc	240
ctnccnaccc	tacntcttcn	nagctgtcn	accctngtn	cgnacccccc	naggtcggga	300
tcgggtttnn	nntgacccng	cnncctcc	ccccntccat	nacgancnc	ccgcaccacc	360
nanngcncg	ncccccgnct	cttcgc	ctgtcctntn	ccccgtngc	ctggcncngn	420
accgcattga	cctcgc	ctnccnngaaa	nognanacgt	ccgggttggn	annancgtg	480
tgggnnngcg	tctgc	gttcc	ccnnc	ccatctt	taingggct	540
ccncgc	tcnnnacnc	cctggacgc	tntc	cccc	ccccccctt	600
cgncgtgncc	cgnc	cc	ntcattt	na	gn	660
cnancngncn	gtcanc	ccnng	ggaagggnng	gn	nnctt	720
cgaanantcc	tcnccn	ccnct	ccggcgn	ctc	ngt	780
ntctccccc	ngngcnc	tcag	ccncc	ctct	gtc	840
tnaccnntac	gant	ttcgn	ccncc	ctt	tt	872

<210> 24
<211> 815
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(815)
<223> n = A,T,C or G

<400> 24

gcatgcaagc	tttagtattc	tatagngtca	cctaaatanc	ttggc	nta	atggc	nta	60
nctgncttcc	tgtgtcaa	at	gtatacna	ta	natat	gaa	tctnat	120
tcntnccat	gt	aa	ta	ct	na	ta	ntg	180
cgcattcn	gc	nc	ta	ct	na	ta	ntn	240
gcnccctgac	tg	gn	ta	ct	na	ta	ntg	300
aananc	cg	ng	ta	ct	na	ta	ntg	360

aacctgcgtc aganncatca aacntggaa acccgcncc angtnnaagt ngnncanan	420
gatccgtcc agnttnacc atccctcnc agegccccct ttngtgcctt anagngnagc	480
gtgtccnanc cnctcaacat ganacgcgcc agnccancc caattingca caatgtcnc	540
gaaccccta ggggantra tncaaanc caggattgtc cnncangaa atcccncanc	600
cccncctac ccnncttgg gacngtgacc aantccgga gtnccagtcc gccngnctc	660
ccccaccggt nnccntgggg gggtaanct cngnntcanc cngncaggn ntgcnaagga	720
accggncctn ggnngaann ancnnctnga agngccncnt cgtataaccc cccctcncca	780
nccnacngnt agntcccccc cngggtnccg aangg	815

<210> 25
<211> 775
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(775)
<223> n = A,T,C or G

<400> 25

ccgagatgtc tcgctccgtg gccttagctg tgctcgcgct actctctctt tctggcttgg	60
aggctatcca gctactcca aagattcagg ttactcagc tcatccagca gagaatggaa	120
agtcaaattt ctgaatttc tatgtgtctg gtttcatcc atccgacatt gaanttgact	180
tactgaagaa tgganagaga attgaaaaag tggagcattc agacttgtct ttcagcaagg	240
actggctttt ctatctcntg tactacactg aattcacccc cactgaaaaa gatgagtatg	300
cctggcgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca	360
tgttaaggcagn cnncatggaa gtttgaagat gccgcatttg gattggatga attccaaatt	420
ctgcttgctt gcntttaat antgatatgc ntatacacc caccctttat gnccccaaat	480
tgttaggggtt acatnantgt tcncntngga catgatctt ctttataant cnccnttcg	540
aattgcccgt cnccngttn ngaatgttc cnnaaccacg gttggctccc ccaggtcncc	600
tcttacggaa gggcctggc cncttncaa gtttggggga accnaaaaatt tcnctntgc	660
ccnccncca cnntcttng nncncanttt ggaacccttc cnattccct tggcctcnna	720
nccttncta anaaaaacttn aaancgtngc naanntttn acttcccccc ttacc	775

<210> 26
<211> 820
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(820)
<223> n = A,T,C or G

<400> 26

anattantac agtgtaatct tttccagag gtgtgtanag ggaacggggc ctagaggcat	60
cccanagata ncttatanca acagtcttt gaccaagac tgctggcac atttcctgca	120
aaaaagtgg cggtccccat cactcctctt ctcctatagc catccagag gggtagtag	180
ccatcangcc ttcgggtggg gggagtcang gaaacaacan accacagacg anacagacca	240
ntgatgacca tggcgggag cgagccctt ccctgnaccc gggtggcana nganageccta	300
nctgagggt cacactataa acgttaacga cnagatnan cacctgttc aagtgcaccc	360
ttcctacctg acnaccagng accnnnaact gengcctggg gacagcnctg ggancagcta	420
acnnagact cacctgcccc cccatggccg tncgcntccc tggcctgnc aaggaaagct	480
ccctgttggaa attncgggaa naccaaggaa nccccctcct ccanctgtga aggaaaaann	540
gatggaaattt tncccttccg gcnntcccc tcttccttta cacgccccctt nntactcncc	600
tccctctntt ntccctgnncn acytttacc cnnnnatttc ccttnattga tcggannctn	660
ganattccac tnnccctncc cnctnacnng naanacnaaa nactntctna cccngggat	720
gggnncctcg ntcatcctct cttttcnctt accncnnntt ctttgctct cctngatca	780

tccaaacntc gntggccntr ccccccnnn tccttnccc	820
<210> 27	
<211> 818	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(818)	
<223> n = A,T,C or G	
<400> 27	
tctgggtat ggccctttcc tcctcaggga cctctgactg ctctggcca aagaatctct	60
tgttttctt ccgagccca ggcaggggtg attcagccct gcccaacctg attctgatga	120
ctggatgc tttgacggac ccaaggggca aatagggtcc cagggccag ggaggggcgc	180
ctgtgagca ctcccgcccc tcaccctgcc cagccctgc catgagctct gggctgggtc	240
tccgcctcca gggttctgtcttccangca ngccancaag tggcgctggg ccacactggc	300
ttcttcgtgc ccnccctgtc getctgantc ttgtcttcc tgcctgtgc angcnccttg	360
gatctcagt ttccctnctc anngaatctt gtttctgann ttttcantta actntgant	420
tatnaccnan tggncgttnc tgcnnactt taatggccn gaccggctaa tccctccctc	480
nctcccttcc anttcnnnnna accngcttnc cncntctcc ccntancccg cnngggaaanc	540
ctcccttgccttcc accncccttcc ggcnnnacccg ccnccnnctt gggggcnnng gtnnctnenc	600
ctgnntnnccc cnctcnccnt tncctcgcc cnccnnccgn nngcannttc ncngtccnn	660
tnnctcttcc ngtntcgnaa ngntcnctn tnnnnnnncn ngntnntncn tccctctcnc	720
cnnntgnang tnnnccnnnc ncnngnccccc nnncnnnnn nggnnnntnnn tctncnengc	780
ccnnccccc ngnattaaagg cctccnnctc cggccnc	818
<210> 28	
<211> 731	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(731)	
<223> n = A,T,C or G	
<400> 28	
aggaagggcg gagggatatt gtangggatt gagggatagg agnataangg gggaggggttg	60
tcccaacatg anggtgnngt tctctttga angagggttg ngttttann cncgggtgggt	120
gattnaaccctt cattgtatgg agnnaaaggtn ttttagggat tttccggctc ttatcgtat	180
ntanattccctt gtnaatcgga aaatnatntt tcnncnggaa aatnttgctc ccatccgnaa	240
attnctcccg gtagtgcatt ntnggggn cngccangtt tcccaggctg ctanaatcgt	300
actaaagntt naagtgggan tncaaattgaa aacccnncc acagnatccn taccggactg	360
tnnnnttccctt cgccctntg actctgcnn agcccaatac ccnnngnat gtcncccn	420
nnngcncnc tgaannnnc tgcngctnn gancatcang gggtttcgca taaaagcnn	480
cgtttcncat naaggcactt tngccatc caaccnctng ccctcnccca ttngccgtc	540
nggttccctt acgctnnntng cnccnnntn ganatttnc cccgcctnggg naancctct	600
gnaatggta gggncctntc ttttnaccnn gnggtntact aatcnctnc acgcnctt	660
tctcnacccccc ccccttttta caatcccanc ggcnaatggg gtctccccnn cganggggg	720
nnnccannc c	731
<210> 29	
<211> 822	
<212> DNA	
<213> Homo sapien	

<220>
 <221> misc_feature
 <222> (1)...(822)
 <223> n = A,T,C or G

<400> 29

actagtccag	tgtggtgaa	ttccattgtg	ttggggncnc	ttctatgant	antnttagat	60
cgctcanacc	tcacancctc	ccnacnangc	ctataangaa	nannaataga	nctgtncnnt	120
atntntacnc	tcatannct	cnnnacccac	tccctttaa	cccntactgt	gcctatngcn	180
tnnctantct	ntgccgctn	cnanccacn	gtgggcccac	cncnngnatt	ctcnatctcc	240
tcnccattn	gcctananta	ngtnccatacc	ctatacctac	nccaatgcta	nnnctaancn	300
tccatnatt	annntaacta	ccactgacnt	ngactttcnc	atnanctct	aatttgaatc	360
tactctgact	cccacngcct	annnattagc	ancntcccc	nacnatntct	caaccaaattc	420
ntcaacaacc	tatctanctg	ttcnccaaacc	nttnccctcg	atccccnnac	aaccccccctc	480
ccaaatacc	nccacctgac	ncctaaccn	caccatcccg	gcaaggcnen	ggncatttan	540
ccactggaat	cacnatngga	naaaaaaaaac	ccnaactctc	tancncnnat	ctccctaana	600
aatnctctn	naatttactn	ncantnccat	caanccacn	tgaaacnnaa	cccctgttt	660
tanatccctt	ctttcgaaaa	ccnaccctt	annncccaac	cttngggcc	cccccnctnc	720
ccnaatgaag	gncccaat	cnangaaacg	ncntgaaaa	ancnaggcna	anannntccg	780
canatcctat	cccttanttn	ggggncccctt	ncccnngggcc	cc		822

<210> 30
 <211> 787
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(787)
 <223> n = A,T,C or G

<400> 30

cggccgcctg	ctctggcaca	tgcctcctga	atggcatcaa	aagtgatgg	ctgcccattg	60
ctagagaaga	ccttctctcc	tactgtcatt	atggagccct	gcagactgag	ggctcccctt	120
gtctgcagga	tttgcgtct	gaagtgcgt	agtgtggctt	ggagctcetc	atctacatna	180
gctgaaagcc	ctggaggggcc	tctctgcct	gcctccccc	tctctccacg	ctctccangg	240
acaccagggg	ctccaggcag	cccattattc	ccagnangac	atggtgttcc	tccacgcgg	300
cccatggggc	ctgnaaggcc	agggtctcct	ttgacaccat	ctctccgc	ctgcctggca	360
ggccgtggga	tccactantt	ctanaacgg	cgccaccncg	gtgggagctc	cagctttgt	420
tcccnttaat	gaaggtaat	tgcncgctt	gctaatcat	ngtgcanaac	tntttcctgt	480
gtgaaattgt	ttntccctc	ncnattccnc	ncnacatacn	aacccggaan	cataaaagtgt	540
taaagcttgg	gggtngcctn	nngaatnaac	ttaactcaat	taattgcgtt	ggctcatggc	600
ccgcttccn	ttcnggaaaa	ctgtcntccc	ctgcnttnt	gaatggcca	ccccccnggg	660
aaaagcggtt	tgcnttttng	ggggntccctt	ccncttcccc	cctcnctaan	ccctncgcct	720
cggtcgtn	ngtngcggg	gaanggnat	nnnctccnc	naaggggng	agnnnngntat	780
ccccaaa'						787

<210> 31
 <211> 799
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(799)
 <223> n = A,T,C or G

<400> 31

tttttttttt tttttttggc gatgctactg ttaattgca ggaggtgggg gtgtgtgtac	60
catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc	120
aacaaaggac tcctgcagcc ttctctgtct gtctcttggc gcaggcacat ggggaggcct	180
cccgccagggt gggggccacc agtccagggg tgggagcact acanggggtg ggagtgggtg	240
gtggctggtn cnaatggcct gncacanatc cctacgattc ttgacacactg gatttcacca	300
ggggacccctc ttttctccca ngnnaacttc nttnatctn aaagaacaca actgtttctt	360
cngcanttct ggctgttcat ggaaagcaca ggtgtccnat ttnggctggg acttggtaca	420
tatggttccg gcccacactc cccntcnaan aagtaattca ccccccccn cnctctntt	480
cctggccct taantaccca caccgaaact canttanta ttcatcttng gntgggcttg	540
nttnatcncn cctgaangcg ccaagttgaa aggccacgccc gtncnnctc cccatagnan	600
nttttncnt canctaattgc ccccccnggc aacnatccaa tcccccccn tgggggcccc	660
agcccanggc ccccgncctg ggnncnccn cncgnantcc ccaggnctc ccantcngnc	720
ccnnngcncc cccgcacgca gaacanaagg ntngagccnc cgcannnnn nngtnnncnac	780
ctcgcccccc cnncgnng	799

<210> 32
<211> 789
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(789)
<223> n = A,T,C or G

<400> 32

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	60
ttttncnag ggcagggtta ttgacaacct cncgggacac aancaggctg gggacaggac	120
ggcaacaggc tcggcggcg gccggccgg ccctacactgc ggtaccaa at ntgcagccctc	180
cgctcccgct ttagtttctt ctgcagctgc aggtatccnt aaaacaggc ctcggccntn	240
ggtgggcacc ctgggattn aattttccacg ggcacaatgc ggtcgcancc ctcaccacc	300
nattaggaat agtggtnna cccnccnccg ttggcnact cccntggaa accacttntc	360
gcccgtcccg catctggct taaacacttgc aaacnctggg gcccctttt tggttantnt	420
nccngccaca atcatnactc agactggcnc gggctggccc caaaaaancn ccccaaaaacc	480
ggncatgtc ttnncggggt tgctgcnatn tncatcacct cccgggnca ncaggncnac	540
ccaaaaatgc ttngggcccn caaaaaanct ccggggggnc ccagttcaa caaatgcatac	600
cccttggcc cccaaatcc ccccccgnnt nctgggtttt ggaaccacg cctctnnctt	660
tggnngccaa gntggntccc cttcgggccc cccgggtggc cccnctctaa ngaaaacncc	720
ntctnnnca ccatcccccc nnngnacgncc tancaangna tcccttttt tanaaacggg	780
ccccccncg	789

<210> 33
<211> 793
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(793)
<223> n = A,T,C or G

<400> 33

gacagaacat gtggatggg ggagcacctt tctatacgac ttacaggaca gcagatgggg	60
aattcatggc tggatggagca atanaacccc agttctacga gctgctgatc aaaggacttg	120
gactaaatgc ttagtgcactt cccaaatcaga tgagcatgga tgattggcca gaaatgaana	180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtgggtcaatctttgacg	240
gcacagatgc ctgtgtgaat ccgggtctga cttttgagga ggttggatcat catgatcaca	300
acaangaacg gggctcgat atcaccantg aggagcagga cgtgagcccc cgccctgcac	360

ctctgtgtt aaacacccca gccatccctt cttcaaaaag ggatccacta cttctagagc	420
ggncgcacc ggggtggagc tccagcttt gtccctta gtgagggtta attgcgcgt	480
tggcgtaatc atggcatan ctgtttctg tgtgaaattt ttatccgctc acaattccac	540
acaacatacg anccggaagc atnaaattt aaagcctggn ggtngctaa tgantgaact	600
nactcacatt aattggctt gcgctcaactg cccgctttcc agtccggaaa acctgtcctt	660
gccagctgcc nttaatgaat cnngccaccc cccggggaaa aggcngrttg cttnttgccc	720
cgcnctccc gcttctcgc ttctgaant cttcccccc ggtcttcgg cttgcggcna	780
acggtatcna cct	793

<210> 34
<211> 756
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(756)
<223> n = A,T,C or G

<400> 34

ggcgcgaccg gcatgtacga gcaactcaag ggcgagtgga accgtaaaag ccccaatctt	60
ancaagtgcg gggaaanagct gggtcgactc aagcttagtt tcctggagct caacttcttg	120
ccaaccacag ggaccaagct gaccaaacag cagctaattc tgcccgtga catactggag	180
atcggggccc aatggagcat cttacgcaan gacatcccct cttcgagcg ctacatggcc	240
cagctcaaattt gctactactt tgattacaan gaggcgtcc ccgagtcage ctatatgcac	300
cagctttgg gcctcaacct cttcttcctg ctgtcccaga accgggtggc tgantnccac	360
acgganttgg ancggctgcc tgcccaanga catacanacc aatgtctaca tcnaccacca	420
gtgtccctgga gcaataactga tgganggcag ctaccncaa gtnttccctgg ccnagggtaa	480
catccccccgc cgagagctac accttcttca ttgacatcct gctcgacact atcagggtatg	540
aaaatcgcn ggttgcctca gaaaggctnc aanaanatcc tttcnctga aggcccccg	600
atncnctagt nctagaatcg gcccgcacat ggggtgganc ctccaacctt tctgttncct	660
ttactgaggg ttnattgccc cccttggcgt tatcatggtc acnccngttn cctgtgttga	720
aattnttaac ccccccacaat tccacgcccna catng	756

<210> 35
<211> 834
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(834)
<223> n = A,T,C or G

<400> 35

ggggatctct anatcnacct gnatgtatgg ttgtcggtgt ggtcgctgtc gatgaanatg	60
aacaggatct tgcccttgaa gctctcggt gctgtnttta agttgcttag tctgcccgtca	120
tagtcagaca cnctcttggg caaaaaacan caggatntga gtcttgattt cacctccaaat	180
aatcttcnng gctgtctgtc cggtgaactc gatgacnang ggcagctgtt tgggtntgat	240
aaantccanc angtttctt tggtgacccctt cccttcaaag ttgttccggc cttcatcaaa	300
cttctnnaan angannanc canctttgtc gagctggnat ttgganaaca cgtcaactgtt	360
ggaaactgtat cccaaatggt atgtcatcca tcgcctctgc tgcctgcaaa aaacttgctt	420
ggcncaaatac cgactccccn tccttggaaag aagccnatca cccccccctc cctggactcc	480
nncaangact ctnccgctnc cccntccnng cagggttgggt ggcannccgg gcccncgtc	540
ttcttcagcc agttcacnat nttcatcagc ccctctgcca gctgttntat tccttgggg	600
ggaancggc tctcccttcc tgaannaact ttgaccgtng gaatagccgc gcntcnccnt	660
acntnctggg cgggttcaa antccctccn ttgnccnntcn cctcgccca ttctggattt	720
nccnaacttt ttcttcccc cncccnccgg ngtttggntt tttcatnggg ccccaactct	780

gctnttggcc antcccctgg gggcntntan cnccccctnt ggtcccnntng ggcc	834
<210> 36	
<211> 814	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(814)	
<223> n = A,T,C or G	
<400> 36	
cggnncgttt ccngccgcgc cccgtttcca tgacnaaggc tcccttcang ttaaatacnn	60
cctagaaaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgccca	120
naacgccaac tcaggccatt cctaccaaag gaagaaaaggc tggctctcc acccccctgt	180
ggaaaggcct gccttgaag acaccacaat ncggctgaat cttaagtctt gtgtttact	240
aatggaaaaa aaaaataaaac aanaggttt gttctcatgg ctgcccaccc cagcctggca	300
ctaaaacanc ccagcgctca cttctgttg ganaaaatatt ctttgcgttt ttggacatca	360
ggcttgcgtt tatcaactgccc acnnttccac ccagctgggc nccctccccc catntttgtc	420
antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc	480
aggggangtc nttnccatgt gatctgcca anantacccn tatcatcnnt gaataaaaag	540
gcccctgaac ganatgcttc cancancctt taagacccat aatccctngaa ccatggtgc	600
cttccggctc gatccnaaag gaatgttctt gggtcccant ccctcccttg ttncttacgt	660
tgtnttggac contgctngn atnacccaan tganatcccc ngaagcaccc tncccctggc	720
atttgaantt cntaaattct ctgcctactn nctgaaagca cnattccctn ggcncnnaan	780
ggngaaactca agaaggctcn ngaaaaacca cncn	814
<210> 37	
<211> 760	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(760)	
<223> n = A,T,C or G	
<400> 37	
gcatgtcgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaaggcg	60
gcfgcagtgtt cgctgaaggg gttgttagtac cagcgcggga tgctctcctt gcagagtcct	120
gtgtctggca ggtccacgca atgccccttg tcaactgggg aatggatgcg ctggagctcg	180
tcnaanccac tcgtgttattt ttcacangca gcctccctcg aagcnccgg gcagttgggg	240
gtgtcgctac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt	300
gggctgacag gtgccagaac acactggatn gcctttcca tggaaaggcc tggggggaaat	360
cncctnancc caaactgcct ctc当地 aaccgcata cccgcacagg ctagaaatgc	420
actcttc当地 ccaaaggtag ttgttcttg tgcccaagca ncctccanca aacccaaaanc	480
ttgcaaaatc tgctccgtgg gggcatnnn taccanggtt gggaaanaa accggcngn	540
ganccnccctt gttgaatgc naaggnaata atcctcctgt cttgcttggg tggaaagca	600
caattgaact gtaacnttgc ggc当地 gtc当地 aatcaccgtc	660
actggaaaaa ggtangtgcc ttcccttgaat tcccaaantt cccctngntt tgggttnntt	720
ctc当地 ctaaaaatcg nt当地 cccntangcg	760
<210> 38	
<211> 724	
<212> DNA	
<213> Homo sapien	

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<220>
<221> misc_feature
<222> (1)...(724)
<223> n = A,T,C or G

<400> 38
tttttttttt tttttttttt tttttaaaaaa cccccccat tgaatgaaaaa      60
cttccnaaat tgtccaaccc cctcnccaa atnnccattt ccgggggggg gttccaaacc 120
caaattaatt ttggantta aattaaatnt tnatnnggg aanaanccaa atgtnaagaa 180
aatttaaccc attatnaact taaatncctn gaaaccnctg gnntccaaaa atttttaacc 240
cttaaatccc tccgaaattt ntaangggaa accaaattcn cctaaggctn tttgaagggtt 300
ngattnaac ccccttnant tnttttacc cnngnctnaa ntatttngnt tccgggtgtt 360
tcctnttaan cntnggtAAC tcccgnata gaannncctt aanccaatta aaccgaattt 420
tttttgaatt ggaaattccn nggaaatttNA cccgggtttt tcccnnttgg gggccatncc 480
cccncttgc gggtttgggn nttagtgaa tttttnnang ncccaaaaaa ncccccana 540
aaaaaaactcc caagnnttaa ttngaatntc ccccttccca ggcctttgg gaaaggnggg 600
tttntggggg ccnngggantt cntcccccn ttncncccc ccccccnggt aaanggttat 660
ngnnttttgtt ttttgggccc cttnanggac ctccggatn gaaattaaat ccccggnncg 720
gccg                                724

<210> 39
<211> 751
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(751)
<223> n = A,T,C or G

<400> 39
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caacacaata tttatttcat ttgtttcttt tatttcattt tatttgggtt ctgctgctgt 120
tttatttattt tttactgaaa gtgagaggga acttttggg cctttttcc tttttctgt 180
ggccgcctta agctttctaa atttggaaaca tctaagcaag ctgaangggaa aaggggggtt 240
cgcaaaatca ctcggggaa nggaaagggtt gctttgttaa tcatgccccta tgggggtga 300
ttaactgctt gtacaattac ntttcaactt taattaattt tgctnaangc tttattana 360
cttgggggtt ccctccccan accaaccnccn ctgacaaaaaa gtgcncgccc tcaaattnatg 420
tcccgcnnt cntgaaaca cacngengaa ngttctcatt ntcccnncnc caggtaaaaa 480
tgaagggtta ccatntttaa cnccacctcc acntggcnnc gcctgaatcc tcnaaaancn 540
ccctcaancn aattnctnng ccccggtcnc gentnngtcc cncccccngt cgggaantn 600
cacccccnga anncnntnnnc naacnaaattt ccgaaaaatat tcccnntcnc tcaattcccc 660
cnnagactnt cctcnncnan cncaattttc ttttnntcac gaacncgnnc cnnaaaatgn 720
nnnnncnccctc cnctngtccn naatcnccan c                                751

<210> 40
<211> 753
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(753)
<223> n = A,T,C or G

<400> 40
gtggtatttt ctgtaaagatc aggtgttcct ccctcgtagg ttttagaggaa acaccctcat      60
agatgaaaac ccccccggaga cagcagcact gcaactgcca agcagccggg gttaggagggg 120

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cgccttatgc acagctggc cttgagaca gcaggcgttc gatgtcaggc tcgatgtcaa	180
tggctggaa gcggcgctg tacctcgta gggcacacc gtcagggccc accaggaact	240
tctcaagtt ccaggcaacn tcgttgcac acaccggaga ccaggtgatn agcttgggt	300
cggcataan cgccgtggcg tcgtcgctgg gagctggcag ggcctccgc aggaaggcna	360
ataaaaggtg cgcccccgca ccgttcanct cgcacttctc naanaccatg angttggct	420
cnaaccacc accannccgg acttccttga nngaattccc aaatcttgc gntcttggc	480
ttctnctgat gccctanctg gttgccnng atgccaanca nccccaanc cccgggtcct	540
aaancaccn cctcctcntt tcatctgggt tntntccccc ggacntggg tccctctcaag	600
gganccata tctcnaccan tactcacnnt nccccccnt gnnacccanc cttctannngn	660
ttcccncgg ncctctggcc cntcaaanan gttncacna cctgggtctg cttcccccc	720
tncccttatct gnaccccnncn tttgtctcan tnt	753

<210> 41
<211> 341
<212> DNA
<213> Homo sapien

<400> 41	
actatatcca tcacaacaga catgcttcat cccatagact tcttgacata gcttcaaatg	60
agtgaaccca tccttgattt atatacatat atgttctcag tattttggga gcctttccac	120
ttctttaaac ctgttcattt atgaacactg aaaataggaa ttgtgagaaga gttaaaaagt	180
tatagcttgt ttacgttagta agttttgaa gtctacattt aatccagaca cttagtttag	240
tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat	300
ttttacttt tgattaattt tgttttatattt attaggtag t	341

<210> 42
<211> 101
<212> DNA
<213> Homo sapien

<400> 42	
acttactgaa tttagttctg tgctttcct tattttagtgt tgtatcataa atactttcat	60
gtttcaaaca ttctaaataaa ataatttca gtggcttcat a	101

<210> 43
<211> 305
<212> DNA
<213> Homo sapien

<400> 43	
acatcttgt tacagtctaa gatgtttct taaatcacca ttcttcctg gtcctcaccc	60
tccagggtgg tctcacactg taatttagagc tattgaggag tctttacagc aaattaagat	120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaggct aagaaaccca	180
cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat	240
tggatacaga acgagagttt tcctggataa ctcagagctg agtacctgcc cggggccgc	300
tcgaa	305

<210> 44
<211> 852
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(852)
<223> n = A,T,C or G

<400> 44

acataaaat cagagaaaag tagtcttga aatatttacg tccaggagtt ctttgttct	60
gattatttg ttgtgtttt ggttgtgtc caaagtattt gcagcttcag ttttcattt	120
ctctccatcc tcggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgt	180
ccagaatttc tctttgttag taatatctca tagctcggtc gagctttca taggtcatgc	240
tgcgtgtt ctctttta ccccatacgct gagccactgc ctctgatttca aagaacctga	300
agacgcctc agatcggtct tcccattta ttaatcctgg gttctgtct gggttcaaga	360
ggatgtcgcg gatgaattcc cataagttag tccctctcg gttgtctt ttgggtgtggc	420
acttggcagg ggggtcttgc tcctttca tacagggtga ctctgcaaca ggaagggtgac	480
tgggtgttgc catggagatc tgagccggc agaaagtttt gctgtccaac aaatctactg	540
tgctaccata gttgggtgtca tataaatagt tctngtctt ccaggtgttc atgatgaaag	600
gctcaggtttgc ttctgttgc acaatgacat tttgtgttgc ctggAACAGGGTCAACTG	660
actggccgtt ccacttcaga tgctgcaagt tgctgttagag gagntgcccc gccgtccctg	720
ccggccgggtt gaactccgtc aaactcatgc tgcaaaagggtt ctcggcgttgc atgtcgaaact	780
cntggaaagg gatacaatttgc gatccagct gttgggtgtc caggagggtga tggagccact	840
cccacacctgt	852

<210> 45
<211> 234
<212> DNA
<213> Homo sapien

<400> 45	
acaacagacc ctgtctcgat aacgacactca tgctcatcaa gttggacgaa tccgtgtcg	60
agtctgacac catccggagc atcagcatttgc ctgcgcgttgc ccctaccgcg gggaaacttt	120
gcctcggttgc tggctgggttgc ctgctggcga acggcagaat gcctaccgttgc ctgcgtgcg	180
tgaacgtgtc ggtgggtgtct gaggagggtct gcagtaagct ctatgaccgc ctgt	234

<210> 46
<211> 590
<212> DNA
<213> Homo sapien

<220>	
<221> misc_feature	
<222> (1)...(590)	
<223> n = A,T,C or G	
<400> 46	
actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atgggtgtgtt	60
atttgatagc aatattttgg agattacaga gtttttagtaa ttaccaatta cacagttaaa	120
aagaagataa tatattccaa gcanatacaa aatatctaattt gaaagatcaa ggcaggaaaa	180
tgcgtgttgc tggaaatca attttatgtt gatggcaca ttatccttta	240
aaagctttca aaanaaaaatttgcgtt ctatgtttaattt caaacagtgt taaaatggat	300
caggataaaan aactgaaggg canaaagaat taattttcac ttcatgttaac ncacccanat	360
ttacaatggc taaaatgcan ggaaaagca gtggaaatgtt ggaagtantc aagggttttc	420
tggctcttac tctgccttac tctttgggttgc tggctttgttgc cctctggaga cagctgccag	480
ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgtt	540
gccttcctt gaggagactt catctcaactg gccaacactc agtcacatgtt	590

<210> 47
<211> 774
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(774)
<223> n = A,T,C or G

<400> 47

acaagggggc ataatgaagg agtggggana gatttaaag aaggaaaaaa aacgaggccc	60
tgaacagaat ttctgnac aacgggctt caaaataatt ttcttggga gggtcaagac	120
gtttcactgc ttgaaactta aatggatgtg gagacanaatt ttctgtaatg accctgaggg	180
cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaagg ctaatccaa	240
aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagttt ccagggctct	300
cctcatccct ggaggacgac agtggaggaa caactgacca tgcctccagg ctccctgttg	360
ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgctgat cctgcgtggc	420
ccacactcct tgaacacaca tccccaggtt atattcctgg acatggctga acctcctatt	480
cctacttcgg agatgccttgc ctcctgcag cctgtcaaaa tcccaactcac cctccaaacc	540
acggcatggg aagccttct gacttgcctg attactccag catttggaa caatccctga	600
ttccccactc ctagaggca agatagggtg gtttagagta gggctggacc acttggagcc	660
aggctgctgg ctccaaattt tggctcattt acgagctatg ggaccttggg caagtnatct	720
tcacttctat ggcnctcatt ttgttctacc tgcaaaatgg gggataataa tagt	774

<210> 48
<211> 124
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(124)
<223> n = A,T,C or G

<400> 48

canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt	60
ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact	120
tggt	124

<210> 49
<211> 147
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(147)
<223> n = A,T,C or G

<400> 49

gccgatgcta ctattttatt gcaggagggtg ggggttttt tattattctc tcaacagctt	60
tgtggctaca ggtgggtct gactgcatna aaaantttt tacgggtgat tgcaaaaatt	120
ttagggcacc catatccaa gcantgt	147

<210> 50
<211> 107
<212> DNA
<213> Homo sapien

<400> 50

acattaaatt aataaaagga ctgttgggt tctgctaaaa cacatggctt gatatattgc	60
.atggtttgag gtagggagga gttaggcata tgttttggg gagggggt	107

<210> 51
<211> 204
<212> DNA

<213> Homo sapien

<400> 51
 gtccttaggaa gtctaggggaa cacacgactc tgggtcacg gggccgacac acttgcacgg 60
 cgsgaaggaa aggagagaaa gtgacaccgt cagggggaaa tgacagaaaag gaaaatcaag 120
 gccttgcagaag gtcagaaaagg ggactcaggg ctcccaccac agccctgccc cacttggcca 180
 cttccctttt gggaccagca atgt 204

<210> 52
 <211> 491
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(491)
 <223> n = A,T,C or G

<400> 52
 acaaagataa catttatctt ataacaaaaaa tttgatagtt ttaaaggtta gtattgtgt 60
 gggtattttc caaaaagacta aagagataac tcaggtaaaa agtttagaaat gtataaaaaca 120
 ccatcagaca ggtttttaaa aaacaacata ttacaaaatt agacaatcat cttaaaaaaaa 180
 aaaacttctt gtatcaattt cttttgttca aatgactga cttaantatt tttaaatatt 240
 tcanaaacac ttccctcaaaa attttcaana tgtagcttt canatgncc ctcagtcccc 300
 atgtagtgcata gataaataaaa tctcgtaga acttaccacc caccacaagg tttctggggc 360
 atgcaacagt gtctttctt tncttttctt tttttttttt ttacaggcac agaaactcat 420
 caattttatt tggataacaa agggtctcca aattatattt aaaaataaat ccaagttat 480
 atcactcttg t 491

<210> 53
 <211> 484
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(484)
 <223> n = A,T,C or G

<400> 53
 acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga 60
 gtattaacag ttgtgaagt ttggatattt tatgcagcat tttcttttg ctttgataac 120
 actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct 180
 caatcaaatac tctacataac actatagtaa tttaaacgtt aaaaaaaaaagt gttgaaatct 240
 gcaactatgat anaccgctcc tgtcagata anactgctt ggaacagaaa gggaaaaanc 300
 agcttgant ttctttgtgc ttagtangagg aaaggctgaa ttaccttggt gctctccct 360
 aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt ctttccncg 420
 tancttgant ctgtgtattc caggancagg cgatggaaat gggccagccc ncggatgttc 480
 cant 484

<210> 54
 <211> 151
 <212> DNA
 <213> Homo sapien

<400> 54
 actaaacctc gtgcttgta actccataca gaaaacggtg ccattccctga acacggctgg 60
 ccactggta tactgctgac aaccgcaaca acaaaaacac aaatccttgg cactggctag 120

tctatgtcct ctcaagtgcc tttttgttg t	151
<210> 55	
<211> 91	
<212> DNA	
<213> Homo sapien	
<400> 55	
acctggcttg tctccgggtg gttccggcg ccccccacgg tccccagaac ggacacttgc	60
gcctccagg gataactcga gccaaagtgg t	91
<210> 56	
<211> 133	
<212> DNA	
<213> Homo sapien	
<400> 56	
ggcggatgtg cggtggttat atacaatat gtcatttat gtaaggact tgagtataact	60
tggatttttg gatatctgtgg gttggggga cggtccagga accaataccc catggataacc	120
aaggacaaac tgt	133
<210> 57	
<211> 147	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(147)	
<223> n = A,T,C or G	
<400> 57	
actctggaga acctgagccg ctgtccgccc tctggatga ggtgatgcan gcngtggcgc	60
gactgggagc tgagcccttc cctttgcgcc tgcctcagag gattttgcc gacntgcana	120
tctcantggg ctggatncat gcagggt	147
<210> 58	
<211> 198	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(198)	
<223> n = A,T,C or G	
<400> 58	
acagggatat aggtttnaag ttatttgtnat tgaaaatac attgaatttt ctgtatactc	60
tgattacata catttacctt taaaaaaaaga tgaaatctt aattttatg ccatctatta	120
atttaccaat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaacttagtt	180
ttgacttcta agtttggt	198
<210> 59	
<211> 330	
<212> DNA	
<213> Homo sapien	
<400> 59	

acaacaaatg	ggtgtgagg	aagtcttac	agcaaaaactg	gtgatggcta	ctgaaaagat	60
ccattaaaa	ttatcattaa	tgatttaaa	tgacaagtt	tcaaaaactc	actcaatttt	120
cacctgtgct	agcttgcataa	aatgggagtt	aactctagag	caaataatgt	atcttctgaa	180
tacagtcaat	aaatgacaaa	gccaggcct	acaggtggtt	tccagactt	ccagaccagg	240
cagaaggaat	ctattttatac	acatggatct	ccgtctgtgc	tcaaaaatacc	taatgatatt	300
tttcgtctt	attggacttc	tttgaagagt				330
<210>	60					
<211>	175					
<212>	DNA					
<213>	Homo sapien					
<400>	60					
accgtgggtg	ccttctacat	tcctgacggc	tccttcacca	acatctggtt	ctacttcggc	60
gtcggtggct	ccttccttctt	catcctcatac	cagctggtgc	tgctcatcga	ctttgcgcac	120
tcctggaaacc	agcggtggct	gggcaaggcc	gaggagtgcg	attcccgatgc	ctgggt	175
<210>	61					
<211>	154					
<212>	DNA					
<213>	Homo sapien					
<400>	61					
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ggttgttgc	cttcaacagt	atcctccctt	ttccggatct	gctgagccgg	acagcagtgc	120
tggactgcac	agccccgggg	ctccacatttgc	ctgt			154
<210>	62					
<211>	30					
<212>	DNA					
<213>	Homo sapien					
<400>	62					
cgctcgagcc	ctatagtgag	tcgttatttgc				30
<210>	63					
<211>	89					
<212>	DNA					
<213>	Homo sapien					
<400>	63					
acaagtcat	ttagcacccct	ttgctttca	aaactgacca	tcttttatat	ttaatgcttc	60
ctgtatgaat	aaaaatggtt	atgtcaagt				89
<210>	64					
<211>	97					
<212>	DNA					
<213>	Homo sapien					
<400>	64					
accggagtaa	ctgagtcggg	acgctgaatc	tgaatccacc	aataaataaa	ggttctgcag	60
aatcgtgc	tccaggatttgc	gtccttggat	ctgggggt			97
<210>	65					
<211>	377					
<212>	DNA					
<213>	Homo sapien					

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<220>
<221> misc_feature
<222> (1)...(377)
<223> n = A,T,C or G

<400> 65
acaacaanaa ntcccttctt taggccactg atggaaacctt ggaaccccctt tttgatggca      60
gcatggcgtc ctaggccttg acacagcggc tgggggtttgg gctntcccaa accgcacacc      120
ccaaccctgg tctaccacca ntctggcta tgggctgtct ctgccactga acatcaggg      180
tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa      240
ggtgctgttt gtcagccag aaaacagctg cctggcatcc gccgctgaac tatgaacccg      300
tgggggtgaa ctacccccc gaggaatcat gcctggcga tgcaanggtg ccaacaggag      360
gggcgggagg agcatgt      377

<210> 66
<211> 305
<212> DNA
<213> Homo sapien

<400> 66
acgcctttcc ctcagaatttcc agggaaagaga ctgtcgctt cttccctccg ttgttgcgtg      60
agaacccgtg tgcccccttcc caccatattcc accctcgctc catcttgaa ctcaaacacg      120
aggaactaac tgcacccctgg tcctctcccc agtccccagt tcacccctcca tccctcacct      180
tcctccactc taaggatata caacactgccc cagcacaggg gccctgaatt tatgtggtt      240
ttatatatttt ttaataaga tgcactttat gtcattttt aataaagtct gaagaattac      300
tgttt      305

<210> 67
<211> 385
<212> DNA
<213> Homo sapien

<400> 67
actacacacaca ctccacttgc ctttgagaa cactttgtcc cagcacatttta ggaatgctga      60
ggtcggacca gccacatctc atgtgcaaga ttgcccagca gacatcagggt ctgagagtc      120
cccttttaaa aaaggggact tgctaaaaaa agaagtctag ccacgattgt gtagagcagc      180
tgtgctgtgc tggagattca ctttgagag agttctcctc tgagacctga tcttagagg      240
ctggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgctg      300
cctctccca gggccacacc tgccacagg tgcttacagg gcactctcag atgcccatac      360
catagtttct gtgcttagtgg accgt      385

<210> 68
<211> 73
<212> DNA
<213> Homo sapien

<400> 68
acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaaaaa tgaaaataaa      60
gttttttaa tgg      73

<210> 69
<211> 536
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(536)

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<223> n = A,T,C or G

<400> 69

actagccat	tgtggtgaa	ttccattgtg	ttgggggctc	tcaccctcct	ctcctgcagc	60
tccagctt	tgctctgcct	ctgaggagac	catggcccag	catctgat	ccctgctgct	120
cctgctggcc	accctagctg	tggccotggc	ctggagcccc	aaggaggagg	ataggataat	180
cccggtggc	atctataacg	cagacotcaa	tgtatgatgg	gtacagcgtg	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctgcgggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	ttttcgacg	tagaggtggg	360
ccgaaccata	tgtaccaagt	cccagccaa	cttggacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaacagt	tgtgctttt	cgagatctac	gaagttccct	ggggagaaca	480
gaangtccct	gggtgaaatc	caggtgtcaa	gaaatcttan	gatctgtt	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgacccta	acagggccc	tctcagccct	cctaattgacc	tccggcctag	ccatgtgatt	60
tcaattccac	tccataacgc	tcctcataact	agcctacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggc	cttcgatacg	ggataatct	atttattacc	ttagaagttt	tttttttcgc	240
agggattttt	ctgagccctt	taccactcca	gcctagcccc	taccccccac	ctaggagggc	300
actggccccc	aacaggcato	accccgctaa	atcccctaga	agtcccactc	ctaaacacat	360
ccgttattact	cgcattcagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aatttattcaa	agcactgctt	attacaattt	tactgggtct	ctatttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(533)

<223> n = A,T,C or G

<400> 71

agagctata	gtacagtgt	atctcagctt	tgcaaacaca	ttttctacat	agatagta	60
aggtaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gattggttt	120
tgtgat	ttaatgtttt	tggcaccc	ttatatgttt	tccaaactt	cagcagtgtat	180
attat	taacttaaaa	agtggat	tttgggggg	aaaaagaaaa	tctccagcaa	240
taaataaagg	tttgtcatct	ttaaaaatac	agcaatatgt	gactttttaa	aaaagctgtc	300
aaataggtgt	gaccctacta	ataattatta	gaaatacatt	taaaaacatc	gagtacctca	360
agtcagttt	cctgaaaaaa	tatcaaata	aactctttaga	gaaatgtaca	taaaaagaatg	420
cttcgttaatt	ttggagtang	aggtccctc	ctcaat	tat	ttttaaa	480
taaaaaaaaaa	aattcacaac	agtatataa	gctgtaaaat	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(511)

<223> n = A,T,C or G

<400> 72

tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcgtgta	60
aatgaaaagg cttccaggca gttatctgat taaaagaacac taaaagaggg acaaggctaa	120
aagccgcagg atgtctcacac tatancaggc gctatttggg ttggctggag gagctgtgga	180
aaacatggan agattggtgc tgganatcgc cgtggctatt cctcattgtt attacanagt	240
gaggttctct gtgtgcccac tggttgaaa accgttctnc aataatgata gaatagtaca	300
cacatgagaa ctgaaaatggc ccaaaccag aaagaaagcc caactagatc ctcagaanac	360
gcttcttaggg acaataaccg atgaagaaaa gatggcctcc ttgtcccccc gtctgttatg	420
atttctctcc attgcagcna naaaccggtt cttctaagca aacncaggtg atgatggcna	480
aaatacaccc cctcttgaag naccnnggagg a	511

<210> 73

<211> 499

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(499)

<223> n = A,T,C or G

<400> 73

cagtgcgcgc actgggtgccca gtaccagtac caataaacagt gccagtgccca gtgccagcac	60
cagtgggtgc ttcaagtgcgt gtgcgcgcct gaccgcact ctcacatttgc ggctcttcgc	120
tggccttggt ggagctgggt ccagcaccag tggcagctct ggtgcctgtg gtttctccata	180
caagtggat tttagatattt gttaaatctgc ccagtccttc tcttcagcc aggggtgcac	240
ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca	300
ctctgcatttta aatcttatttgc ccatttctga aaaaaaaaaaaa aaaaaaaaaaggg cggccgctcg	360
antcttagagg gcccggtttaa acccgctgtat cagcctcgac tgtgcctct anttgcctcagc	420
catctgttgtt ttggccctcc cccgntgcct tccttgaccct tggaaagtgc cactcccact	480
gtccttcctt aantaaaaat	499

<210> 74

<211> 537

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(537)

<223> n = A,T,C or G

<400> 74

tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat	60
ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact	120
tccaggccca cgctcaagt gaatttgaat actgcatttgc cagtgttagag taacacataa	180
cattgtatgc atggaaacat ggaggaacag tattacagtgc tcctaccact ctaatcaaga	240
aaagaattac agactctgtat tctacagtgc tgattgaatt ctaaaaaatgg taatcattag	300
ggctttgtat ttataanact ttgggtactt atactaaattt atggtagtta tactgccttc	360
cagtttgcattt gatatatttgc ttgatattaa gattcttgac ttatattttg aatgggttct	420
actgaaaaan gaatgatata ttcttgaaga catcgatata catttatttgc cactcttgcatt	480
tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaaa gtcggcgt	537

<210> 75

<211> 467

<212> DNA

<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(467)
<223> n = A,T,C or G

<400> 75
caaananacaat tgttcaaaag atgcaaatacg tacactactg ctgcagctca caaacaccc 60
tgcattttac acgtacccctc tcctgcctt caagtagtgt ggtctatccc gccatcatca 120
cctgctgtct gcttagaaaga acggctttct gctgcaang agagaatca taacagacgg 180
tggcacaagg aggccatctt ttcctcatcg gtattgtcc ctagaagcgt cttctgagga 240
tctagttggg ctttcttct gggtttgggc catttcantt ctcatgtgt tactattcta 300
tcattattgt ataacgggtt tcaaaccngt gggcacncag agaacacctac tctgtataaa 360
caatgaggaa tagccacggg gatctccagg accaaatctc tccatgtnt tccagagctc 420
ctccagccaa cccaaatagc cgctgtatn gtgtagaaca tccctgn 467

<210> 76
<211> 400
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(400)
<223> n = A,T,C or G

<400> 76
aagctgacag catcgggcc gagatgtctc getccgtggc ctttagctgtg ctgcgcgtac 60
tctctctttc tggcctggag gctatccagg gtactccaaa gattcagggt tactcacgtc 120
atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg tttcatccat 180
ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag 240
acttgtctt cagcaaggac tggtcttct atctcttgta ctacactgaa ttccccccca 300
ctgaaaaaaga tgtagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaaagatng 360
ttnagtggga tgcganacatg taagcagcan catgggaggt 400

<210> 77
<211> 248
<212> DNA
<213> Homo sapien

<400> 77
ctggagtgcc ttgggtttc aagccctgc aggaagcaga atgcacccctc tgaggcacct 60
ccagctgccc cggcgggggg tgcgaggctc ggagcacccct tgcccgctg tgattgtgc 120
caggcactgt tcatctcagc tttctgtcc ctttgcctcc ggcaagegct tctgtgtaaa 180
gttcatatatct ggagcctgat gtcttaacga ataaaggctcc catgctccac ccgaaaaaaaaa 240
aaaaaaaaa 248

<210> 78
<211> 201
<212> DNA
<213> Homo sapien

<400> 78
actagtcacatg tgggtggaa ttccatgtg ttggcccaa cacaatggct accttttaaca 60
tcacccagac cccgcctgc cctgtccccc cgctgtgtc aacgacagta tgatgttac 120
tctgtactc ggaaactatt tttatgtat taatgtatgc tttcttgc tttatgtatgc 180
gataaaaaaa aaaaaaaaaa a 201

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<210> 79
 <211> 552
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(552)
 <223> n = A,T,C or G

<400> 79
 tcctttgtt aggttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg 60
 ttaggcagt gctagtaatt tcctcgtaat gattctgttta ttactttcctt attctttattt 120
 cctctttctt ctgaagatta atgaagttga aaattggagggt ggataaaatac aaaaaggtag 180
 tgtgatagta taagtatcta agtgcaagatg aaagtgttta atatataatcc attcaaaattt 240
 atgcaagttta gtaattactc agggtaactt aaattactttt aatatgtgtt tgaacctact 300
 ctgttccttg gctagaaaaaa attataaaca gactttgtt agtttggaa gccaaatttga 360
 taatattcta tgttctaaaaa gttggcttat acataaaanta tnaagaaata tggaaatttta 420
 ttcccaggaa tatgggttc atttatgaat antacccggg anagaagttt tgantnaaac 480
 cngtttttgtt taatacgttta atatgcctn aatnaacaag gcntgactta ttccaaaaaa 540
 aaaaaaaaaaa aa 552

<210> 80
 <211> 476
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(476)
 <223> n = A,T,C or G

<400> 80
 acagggattt gagatgctaa ggccccagag atcggttgc ccaaccctct tattttcaga 60
 ggggaaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct 120
 cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca gcccctgttt 180
 gcaatttcacg ttgcacccctc caacttaaac attcttcata tgtgatgtcc ttagtcacta 240
 aggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac 300
 tcttctaagt cctcttccag cctcactttg agtccttcctt ggggggttgc aggaantntc 360
 tcttggcttt ctcaataaaaaa tctctatcca tctcatgttt aatttggtag gcntaaaaat 420
 gctgaaaaaaaaa ttaaaatgtt ctggttcnc ttaaaaaaaaa aaaaaaaaaa aaaaaaa 476

<210> 81
 <211> 232
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(232)
 <223> n = A,T,C or G

<400> 81
 ttttttttttgcntcn ctgtggngtt attgttgctg ccaccctgga ggagcccagt 60
 ttcttcgtta tctttctttt ctggggatc ttccctggctc tgccccctcca ttcccagcct 120
 ctcatccccca tcttgcactt ttgcttaggggt tgaggcgct ttccctggtag cccctcagag 180
 actcagtcag cggaataag tccttaggggt ggggggtgtg gcaagccggc ct 232

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<210> 82
<211> 383
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

<400> 82
aggcgggagc agaagctaaa gccaaagccc aagaagagtgc cactgggcc 60
agtaccagta ccaataacat gccagtgcga gtgccagcac cagtgggtgc 120
gtgccagcct gaccgcact ctcacatttgc ggctttcgcc tggccttggc 180
ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagttagat 240
gttaatcctg ccagtcttcc tcttcaagcc agggtgcatc ctcagaaaacc 300
agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta 360
ccatttcaaa aaaaaaaaaaaa aaa 383

<210> 83
<211> 494
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(494)
<223> n = A,T,C or G

<400> 83
accgaatttgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca 60
gggagatcga gtctatacgc tgaagaaatt tgacccgatg ggacaacaga cctgctcagc 120
ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa 180
acgcttcaag gtgctcatga cccagcaacc gcgcctgtc ctctgagggt cottaactg 240
atgtcttttc tgccacctgt taccctcggt agactccgtt accaaactct tcggactgtg 300
agccctgtat ccttttgcc agccataactc ttggcncatcc agtctctcgat ggcgattgt 360
tatgcttgtt tgaggcaatc atggtggcat cacccatnaa gggAACACAT ttgantttt 420
tttcncatcat tttaaattac naccagaata ntccagaata aatgaattga aaaaactctta 480
aaaaaaaaaaa aaaa 494

<210> 84
<211> 380
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

<400> 84
gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacggacacg tgacttccca 60
agtatcctgc gcccgtctt ctaccgtccc tacctgcaga tcttcggca gattccccag 120
gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cgccctctgg 180
gcacaccctc ctggggccca ggccggcacc tgctgtccc agtgcctaa ctggctggtg 240
gtgctgtcc tctgtcatctt cctgtctgtg gccaacatcc tgctggtcac ttgctcattt 300
ccatgttcag ttacacatcc ggcaaagtac agggcaacag cnatctctac tggaaaggcc 360
agcgtnccg cctcatccgg 380

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<210> 85
<211> 481
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(481)
<223> n = A,T,C or G

<400> 85
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcg ttcataaccgc      60
tnccatcgta atactgtagg tttgccacca cctcctgcat cttggggcg ctaatatcca      120
ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcg      180
tgtgaaagga tctccagaag gagtgctcga tcttccccac actttgatg actttattga      240
gtcgattctg catgtccagc aggaggtgt accagctctc tgacagttag gtcaccagcc      300
ctatcatgcc nttaaacgtg ccgaagaaca ccgagccttg tgtgggggt gnagtctcac      360
ccagatctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggnngaa      420
aaagaacacc tcctgaaagt gctngccgt cctcgccnt tggtggnngc gcntncctt      480
t                                         481

<210> 86
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

<400> 86
aacatcttcc tgtataatgc tgtgttatcgatcgatccgatn ttgtctgctg agaattcatt      60
acttggaaaa gcaacttnaa gcctggacac tggattaaa attcacaata tgcaacactt      120
taaacagtgt gtcaatctgc tcccttactt tgcattcacc agtctggaa taagggatg      180
ccctattcac acctgttaaa agggcgctaa gcattttga ttcaacatct ttttttttga      240
cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gtttagccaat tcactttctt      300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg      360
atatntgagc ggaagantag cctttctact tcaccagaca caactcctt catattggga      420
tgttnacnaa agttatgtct cttacagatg ggatgcttt gtggcaattc tg      472

<210> 87
<211> 413
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(413)
<223> n = A,T,C or G

<400> 87
agaaaccagt atctctnaaa acaacctctc ataccttgcgt gacctaattt tgggtgcgt      60
tgtgtgtcg cgcatattat atagacaggc acatctttt tactttgtaaagcttatg      120
cctctttgtt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggactt      180
ttgtcttctg tggaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt      240
tttattcgac atgaagggaaa tttccagatn acaacactna caaactctcc cttgactagg      300

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ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aatncataa	360
acagaaaattg ggtngtatat tgaaananng catcattnaa acgtttttt ttt	413
<210> 88	
<211> 448	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(448)	
<223> n = A,T,C or G	
<400> 88	
cgcagccccgt cctctctatc tagctccagc ctctcgctg ccccactccc cgctgtccgc	60
gtcctagccn accatggccg ggccccgtcg cgccccgtcg ctccgtctgg ccattctggc	120
cgtggccctg gccgtgagcc ccgcggccgg ctccagtcgg ggcaagccgc cgccgtgg	180
gggaggccca tggaccccgc gtggaagaag aagggtgtcg gcgtgactg gactttgccg	240
tccggcnanta caacaaaaccc gcaacnactt ttaccnagcn cgctgtcgag gttgtgccgc	300
cccaancaaa ttgttactng gggtaantaa ttcttggaaat ttgaacctgg gccaaacnng	360
tttaccagaa ccnagccaat tngaacaatt nccctccat aacagccccct tttaaaaagg	420
gaancantcc tgntctttc caaatttt	448
<210> 89	
<211> 463	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(463)	
<223> n = A,T,C or G	
<400> 89	
gaattttgtg cactggccac tgtgatggaa ccattggcc aggatgctt gagtttatca	60
gtagtgattc tgccaaagtt ggtgtttaa catgagtatg taaaatgtca aaaaatttagc	120
agaggtctag gtctgcatat cagcagacag ttgtccgtg tatttttagt ccttgaagtt	180
ctcagtgaca agttnnttct gatgcgaagt tctnattcca gtgttttagt ccttgcac	240
tttnatgttn agacttgct ctntnaaatt gctttgtnt tctgcaggta ctatctgtgg	300
tttaacaaaa tagaannact tctctgcttn gaanattga atatcttaca tctnaaaatn	360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn	420
aattcnnana anttcagntr tcataacaaca naacngganc ccc	463
<210> 90	
<211> 400	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(400)	
<223> n = A,T,C or G	
<400> 90	
agggattgaa ggtctnttnt actgtcgac tggtcaccca ccaactctac aagttgctgt	60
cttccactca ctgtctgtaa gcntnttaac ccagactgtt tcttcataaa tagaacaaat	120
tcttcaccag tcacatcttc taggacctt ttggattcag ttgtataag ctcttccact	180
tcctttgtta agacttcattc tggtaaaagtc ttaagtttg tagaaaggaa tttaattgct	240

cgttctctaa caatgtcctc tccttgaagt atttggctga acaacccacc tnaagtcctc	300
tttgtcatcc attttaata tacttaatag ggcattggtn cactaggta aattctgcaa	360
gagtcatctg tctgaaaag ttgcgttagt atatctgcca	400
<210> 91	
<211> 480	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(480)	
<223> n = A,T,C or G	
<400> 91	
gagctcggt ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact	60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagttagac	120
atgcctctt gactaccgtg tgccagtgc ggtgattctc acacacctcc nnccgcttt	180
tgtggaaaaa ctggcaactt nctggacta gcaagacatc acttacaaat tcacccacga	240
gacacttgaa aggtgttaaca aagcgactt tgcattgctt tttgtccctc cggcaccagt	300
tgtcaatact aacccgctgg tttgcctcca tcacatttgt gatctgtgc tctggataca	360
tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactt ggtgcctgtt	420
ngatcagggtt cccatttccc agtccgaatg ttcacatggc atatnntact tcccacaaaa	480
<210> 92	
<211> 477	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(477)	
<223> n = A,T,C or G	
<400> 92	
atacagccca natcccccca cgaagatgcg cttgttgact gagaacctga tgcggtaact	60
ggtcccgtg tagccccagc gactctccac ctgttggaa cggttgcgc tgcaactcctt	120
cccacgcagg cagcagcggg gccggtaat gaactccact cgtggcttgg gtttgcgggt	180
taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccact gtgcgggacc	240
tgcagcggaaa ctcctcgatg gtcatgagcg ggaagcgaat gangccagg gccttgccca	300
gaacctcccg cctgttctct ggctcacct gcagctgctg cgcctnacac tcggcctegg	360
accagcggac aaacggcggtt gaacagccgc acctcacggg tgcccantgt gtgcgcgtcc	420
aggaacggcn ccagcgtgtc caggtcaatg tcggtaanc ctcccggtt aatggcg	477
<210> 93	
<211> 377	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(377)	
<223> n = A,T,C or G	
<400> 93	
gaacggctgg accttgcctc gcattgtgcgtt gtcggcagga ataccttggc aagcagctcc	60
agtccgagca gccccagacc gctgcccggcc gaagctaagg ctgcctctgg cttcccttc	120
cgcctcaatg cagaaccant agtgggagca ctgtgttttag agttaagagt gaacactgtt	180

tgattttact tggttaattc ctctgttata tagctttcc caatgcta at ttccaaacaa	240
caacaacaaa ataacatgtt tgcctgttna gttgtataaa agtangtgat tctgtatnta	300
aagaaaatat tactgttaca tatactgtt gcaantctg tatttattgg tnctctggaa	360
ataaaatatata tattaaa	377
<210> 94	
<211> 495	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(495)	
<223> n = A,T,C or G	
<400> 94	
ccctttgagg ggttagggtc cagttcccag tggaaagaaac aggccaggag aantgcgtgc	60
cgagctgang cagattccc acagtacccc cagagccctg ggctatagtc tctgaccct	120
ccaaggaaaag accacccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg	180
gaaggccccca ttccggggct gttcccccag gaggaaggga aggggctctg tgtgcccccc	240
acgaggaana ggcctgtant cctgggatca nacaccctt cacgtgtatc cccacacaaa	300
tgcaagctca ccaaggtccc ctctcagttcc ctccctaca ccctgaacgg ncactggccc	360
acacccaccc agancancca cccgcatgg ggaatgtnc caaggaatcg cngggcaacg	420
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<400> 104

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<210> 105
<211> 538
<212> DNA
<213> Homo sapien

<400> 105

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<210> 106
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<212> DNA
<213> Homo sapien

<400> 106

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<210> 107
<211> 1621
<212> DNA
<213> Homo sapien

<400> 107

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<210> 108
 <211> 382
 <212> PRT
 <213> Homo sapien

<400> 108															
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Gly	Lys	Arg	Ser	Leu	Val	Leu	Asp	Leu	Lys	Gln	Pro	Arg	Gly	Ala	Ala
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Val	Leu	Arg	Arg	Leu	Cys	Lys	Arg	Ser	Asp	Val	Leu	Leu	Glu	Pro	Phe
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Arg	Arg	Gly	Val	Met	Glu	Lys	Leu	Gln	Leu	Gly	Pro	Glu	Ile	Leu	Gln
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Arg	Glu	Asn	Pro	Arg	Leu	Ile	Tyr	Ala	Arg	Leu	Ser	Gly	Phe	Gly	Gln
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Gly	Gln	Val	Ile	Asp	Ala	Asn	Met	Val	Glu	Gly	Thr	Ala	Tyr	Leu	Ser
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Thr	Ala	Asp	Gly	Glu	Phe	Met	Ala	Val	Gly	Ala	Ile	Glu	Pro	Gln	Phe
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Tyr	Glu	Leu	Leu	Ile	Lys	Gly	Leu	Gly	Leu	Lys	Ser	Asp	Glu	Leu	Pro
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 Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp
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 Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val
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 His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu
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 Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala
 325 330 335
 Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu
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<210> 109
 <211> 1524
 <212> DNA
 <213> Homo sapien

<400> 109

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<210> 110
 <211> 3410
 <212> DNA
 <213> Homo sapien

<400> 110

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<212> DNA
 <213> Homo sapien

<400> 111

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ccatgcagtg	cttcagcttc	attaagacca	tgtatgatcc	cttcaatttg	ctcatcttc	180
tgtgtggtgc	agccctgttg	gcagtggca	tctgggtgtc	aatcgatggg	gcataccccc	240
tgaagatctt	cggccactg	tgcgtccagtg	ccatgcagtt	tgtcaacgtg	ggctacttcc	300
tcatgcagc	cggcgttgtg	gtctttgtc	ttggtttcc	gggctgtat	ggtgctaaga	360
ctgagagcaa	gtgtgcctc	gtgacgttct	tcttcatcc	cctccatc	ttcattgtcg	420
aggttgcagc	tgcgtggtc	gccttgggt	acaccacaat	ggctgagcac	ttcctgacgt	480
tgctggtagt	gcctgccatc	aagaaaagatt	atggttcccc	ggaagacttc	actcaagtgt	540
ggaacaccac	catgaaagg	ctcaagtgc	gtggcttcc	caactatacg	gattttgagg	600
actcacccata	cttcaaagag	aacagtcct	ttccccat	ctgttcaat	gacaacgtca	660
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gcttcaatca	gttttgtat	gacatccgaa	ctaatgcagt	caccgtgggt	ggtgtggcag	780
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tacaataagt	ccacttctgc	ctctgcccact	actgctgcca	catggaaact	gtgaagaggc	900
accctggcaa	gcagcagtga	ttgggggagg	ggacaggatc	taacaatgtc	acttgggcca	960
gaatggacct	gcctttctg	ctccagactt	ggggcttagat	agggaccact	ccttttagcg	1020
atgcctgact	ttccttccat	tggtgggtgg	atgggtgggg	ggcattccag	agcctctaag	1080
gtagccagtt	ctgttgccca	ttccccca	ctattaaacc	tttgatatgc	cccctagggc	1140
tagtggtgat	cccagtgc	tactggggga	tgagagaaaag	gcattttata	gcctgggcat	1200
aagtgaaatc	agcagagcct	ctgggtggat	gtgtagaagg	cacttcaaaa	tgcataaaacc	1260
tgttacaatg	ttaaaaaaaaaa	aaaaaaaaaa				1289

<210> 112

<211> 315

<212> PRT

<213> Homo sapien

<400> 112

Met	Val	Phe	Thr	Val	Arg	Leu	Leu	His	Ile	Phe	Thr	Val	Asn	Lys	Gln
1	5								10					15	
Leu	Gly	Pro	Lys	Ile	Val	Ile	Val	Ser	Lys	Met	Met	Lys	Asp	Val	Phe
				20				25					30		
Phe	Phe	Leu	Phe	Leu	Gly	Val	Trp	Leu	Val	Ala	Tyr	Gly	Val	Ala	
						35		40			45				
Thr	Glu	Gly	Leu	Leu	Arg	Pro	Arg	Asp	Ser	Asp	Phe	Pro	Ser	Ile	Leu
					50		55			60					
Arg	Arg	Val	Phe	Tyr	Arg	Pro	Tyr	Leu	Gln	Ile	Phe	Gly	Gln	Ile	Pro
					65		70		75				80		
Gln	Glu	Asp	Met	Asp	Val	Ala	Leu	Met	Glu	His	Ser	Asn	Cys	Ser	Ser
					85		90			95					
Glu	Pro	Gly	Phe	Trp	Ala	His	Pro	Pro	Gly	Ala	Gln	Ala	Gly	Thr	Cys
					100		105			110					
Val	Ser	Gln	Tyr	Ala	Asn	Trp	Leu	Val	Val	Leu	Leu	Leu	Val	Ile	Phe
					115		120			125					
Leu	Leu	Val	Ala	Asn	Ile	Leu	Leu	Val	Asn	Leu	Leu	Ile	Ala	Met	Phe
					130		135			140					
Ser	Tyr	Thr	Phe	Gly	Lys	Val	Gln	Gly	Asn	Ser	Asp	Leu	Tyr	Trp	Lys
					145		150			155			160		
Ala	Gln	Arg	Tyr	Arg	Leu	Ile	Arg	Glu	Phe	His	Ser	Arg	Pro	Ala	Leu
					165		170			175					
Ala	Pro	Pro	Phe	Ile	Val	Ile	Ser	His	Leu	Arg	Leu	Leu	Arg	Gln	
					180		185			190					
Leu	Cys	Arg	Arg	Pro	Arg	Ser	Pro	Gln	Pro	Ser	Ser	Pro	Ala	Leu	Glu

195	200	205
His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr		
210	215	220
Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp		
225	230	235
Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val		
245	250	255
Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg		
260	265	270
Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly		
275	280	285
Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly		
290	295	300
Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp		
305	310	315

<210> 113
 <211> 553
 <212> PRT
 <213> Homo sapien

<400> 113		
Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala		
1	5	10
Gln Leu Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu		
20	25	30
Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val		
35	40	45
Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly		
50	55	60
Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly		
65	70	75
Arg Tyr Gly Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile		
85	90	95
Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu		
100	105	110
Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly		
115	120	125
Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu		
130	135	140
Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala		
145	150	155
Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr		
165	170	175
Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu		
180	185	190
Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu		
195	200	205
Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly		
210	215	220
Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His		
225	230	235
Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu		
245	250	255
Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg		
260	265	270
Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe		
275	280	285

Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val
 290 295 300
 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
 305 310 315 320
 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu
 325 330 335
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg
 340 345 350
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala
 355 360 365
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
 370 375 380
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala
 385 390 395 400
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly
 405 410 415
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu
 420 425 430
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala
 435 440 445
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser
 450 455 460
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala
 465 470 475 480
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
 485 490 495
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser
 500 505 510
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala
 515 520 525
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp
 530 535 540
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala
 545 550

<210> 114
 <211> 241
 <212> PRT
 <213> Homo sapien

<400> 114
 Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
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 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
 20 25 30
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
 35 40 45
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
 50 55 60
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
 65 70 75 80
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Ile
 85 90 95
 Phe Ile Ala Glu Val Ala Ala Val Val Ala Leu Val Tyr Thr Thr
 100 105 110
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
 115 120 125
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met

130	135	140													
Lys	Gly	Leu	Lys	Cys	Cys	Gly	Phe	Thr	Asn	Tyr	Thr	Asp	Phe	Glu	Asp
145				150					155				160		
Ser	Pro	Tyr	Phe	Lys	Glu	Asn	Ser	Ala	Phe	Pro	Pro	Phe	Cys	Cys	Asn
							165		170				175		
Asp	Asn	Val	Thr	Asn	Thr	Ala	Asn	Glu	Thr	Cys	Thr	Lys	Gln	Lys	Ala
							180		185			190			
His	Asp	Gln	Lys	Val	Glu	Gly	Cys	Phe	Asn	Gln	Leu	Leu	Tyr	Asp	Ile
							195		200			205			
Arg	Thr	Asn	Ala	Val	Thr	Val	Gly	Gly	Val	Ala	Ala	Gly	Ile	Gly	Gly
							210		215			220			
Leu	Glu	Leu	Ala	Ala	Met	Ile	Val	Ser	Met	Tyr	Leu	Tyr	Cys	Asn	Leu
225					230				235			240			
Gln															

<210>	115					
<211>	366					
<212>	DNA					
<213>	Homo sapien					
<400>	115					
gcttttctc	tcccttcctc	tgaatttaat	tcttcaact	tgcaatttgc	aaggattaca	60
catttcactg	tgtgttatat	tgtgttgc当地	aaaaaaaaaa	gtgtcttgc当地	ttaaaattac	120
ttggtttgc当地	aatccatctt	gtttttccc	cattggact	agtcattaac	ccatctctga	180
actggtagaa	aaacatctga	agagctagtc	tatcagcatc	tgacaggtga	attggatgg	240
tctcagaacc	atttcaccca	gacagctgt	ttctatcctg	ttaataaaat	tagttgggt	300
tctctacatg	cataacaaac	cctgctccaa	tctgtcacat	aaaagtctgt	gacttgaagt	360
tttagtc						366
<210>	116					
<211>	282					
<212>	DNA					
<213>	Homo sapien					
<220>						
<221>	misc_feature					
<222>	(1)...(282)					
<223>	n = A,T,C or G					
<400>	116					
acaaagatga	accatttcct	atattatagc	aaaattaaaa	tctacccgta	ttctaataatt	60
gagaaatgag	atnaaacaca	atnttataaa	gtctacttag	agaagatcaa	gtgacctcaa	120
agactttact	atttcatat	ttaagacac	atgatttac	ctatttagt	aacctggtc当地	180
atacgtaaaa	caaaggataa	tgtgaacagc	agagaggatt	tgttggcaga	aaatctatgt	240
tcaatctnga	actatctana	tcacagacat	ttctattcct	tt		282
<210>	117					
<211>	305					
<212>	DNA					
<213>	Homo sapien					
<220>						
<221>	misc_feature					
<222>	(1)...(305)					
<223>	n = A,T,C or G					
<400>	117					

acacatgtcg cttcaactgcc ttcttagatg cttctggtca acatanagga acagggacca	60
tatttatcct ccctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa	120
aataaggcaa aatatatgaa acaacaggc tcgagatatt ggaaatcagt caatgaagga	180
tactgatccc tgatcaactgt cctaattgcag gatgtggaa acagatgagg tcacctctgt	240
gactccccca gcttaactgcc tgttagagat ttctangctg cagttcagac agggagaaaat	300
tgggt	305
<210> 118	
<211> 71	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(71)	
<223> n = A,T,C or G	
<400> 118	
accaagggtgt ntgaatctct gacgtgggaa tctctgattc ccgcacaatc tgagtggaaa	60
aantcctggg t	71
<210> 119	
<211> 212	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(212)	
<223> n = A,T,C or G	
<400> 119	
actccgggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca	60
gaaaatgggg taaaattggc caactttcta tnaactttagt ttggcaant tgccaccaac	120
agtaagctgg cccttctaataa aaaagaaaaat taaaagggttt ctcactaanc ggaattaant	180
aatggantca aganactccc aggccctcagc gt	212
<210> 120	
<211> 90	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(90)	
<223> n = A,T,C or G	
<400> 120	
actcggtgca natcaggggc ccccccagagt caccgttgca ggagtccttc tggtcttgcc	60
ctccgcggc gcagaacatg ctggggtggt	90
<210> 121	
<211> 218	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	

<222> (1)...(218)
 <223> n = A,T,C or G

<400> 121
 tgtancgtga anacgacaga nagggttgc aaaaatggag aanccttcaa gtcattttga 60
 gaataagatt tgcataaaga tttggggcta aaacatggtt attggagac atttctgaag 120
 atatncangt aaattangga atgaattcat gttcttttgc ggaattcctt tacgatngcc 180
 agcatanact tcatacggtt atancagcta cccttgc 218

<210> 122
 <211> 171
 <212> DNA
 <213> Homo sapien

<400> 122
 taggggtgta tgcaactgta aggacaaaaaa tttagactca actggcttaa ccaataaagg 60
 catttgttag ctcatggaa acggaaatcggtt atgggtgggc atcttcgtt ctgcgttg 120
 caccaccccg gcgggttcat ctgtgccaca ggtccctgtt gacagtgcgg t 171

<210> 123
 <211> 76
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(76)
 <223> n = A,T,C or G

<400> 123
 tgttagcgtga agacnacaga atggtgtgtt ctgtgctatc caggaacaca tttattatca 60
 ttatcaanta ttgtgt 76

<210> 124
 <211> 131
 <212> DNA
 <213> Homo sapien

<400> 124
 acctttcccc aaggccaatg tcctgtgtgc taactggccg gctgcaggac agctgcaatt 60
 caatgtgtcg ggtcatatgg aggggaggag actctaaaat agccaattttt attctcttgg 120
 ttaagatttg t 131

<210> 125
 <211> 432
 <212> DNA
 <213> Homo sapien

<400> 125
 actttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg 60
 cttgaaaaag aggtgatagc tcttcagagg acttgtgact tttgctcaga tgctgaagaa 120
 ctacagtcgt catttggcag aatgaagat gaatttggat taaatgagga tgctgaagat 180
 ttgcctcacc aaacaaaatg gaaacaactg agagaaaaattt ttcaggaaaa aagacagtgg 240
 ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcataact tcatacgatcc 300
 catgggtgggg gtcttgcata tcataagaatg gaattgattt tgctttgca agaatctcag 360
 cagggaaacat cagaaccact atttcttagc cctctgtcag agcaaacctc agtgcctctc 420
 ctctttgtt gt 432

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<210> 126
<211> 112
<212> DNA
<213> Homo sapien

<400> 126
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcaact ttctaaccat      60
agtaagaatg atattcccc ccagggatca ccaaataattt ataaaaattt gt             112

<210> 127
<211> 54
<212> DNA
<213> Homo sapien

<400> 127
accacgaaac cacaacaacat atggaagcat caatccactt gccaaaggcaca gcag      54

<210> 128
<211> 323
<212> DNA
<213> Homo sapien

<400> 128
acctcatttag taattgttt gttgtttcat ttttttctaa tgtctccctt ctaccagctc      60
acctgagata acagaatgaa aatggaaagga cagccagatt tctcccttgc tctctgctca    120
ttctctctga agtcttaggtt acccattttg gggaccattt ataggcaata aacacagtcc   180
ccaaaggcatt tgacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt   240
ttcctgcaaa aggttcactc agtcccttgc ttgctcgtt gactggcgc cccaggccct   300
aggctgcctt cttttccatg tcc                         323

<210> 129
<211> 192
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(192)
<223> n = A,T,C or G

<400> 129
acatacatgt gtgttatattt ttaaatatca cttttgtatc actctgactt tttagcatac      60
tggaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc    120
tagcacattc atctgtgata naaagatagg tgagttcat ttccttcacg ttggccaatg   180
gataaaacaaa gt                         192

<210> 130
<211> 362
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(362)
<223> n = A,T,C or G

<400> 130
cccttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca      60

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tataatgacg caacaaaaag gtgctgtta gtcctatgg tcagttatg cccctgacaa	120
gttccattg tggggcccg atcttctggc taatcggtt atcctccatg ttatttagtaa	180
ttctgtattc cattttgtta acgcctggta gatgtAACCT gctangaggc taactttata	240
cttatttaaa agcttcttatt ttgtggcat taaaatggca atttatgtgc agcactttat	300
tgcagcagga agcacgtgtg gggtgggtt aaagctctt gctaatttta aaaagtaatg	360
gg	362
<210> 131	
<211> 332	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(332)	
<223> n = A,T,C or G	
<400> 131	
ctttttgaaa gatcggtgtcc actcctgtgg acatcttgtt ttaatggagt ttcccattgca	60
gtangactgg tatgggtgca gctgtccaga taaaacatt tgaagagctc caaaatgaga	120
gttctccag gtgcgcctg ctgcctcaag ttcagcagc agcctctttt aggaggcatc	180
ttctgaacta gattaaggca gcttgtaaat ctgtatgtat ttgggttatt atccaactaa	240
cttccatctg ttatcactgg agaaagcccc aactccccan gacnggtacg gattgtggc	300
atanaaggat tgggtgaagc tggcggtgtg gt	332
<210> 132	
<211> 322	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(322)	
<223> n = A,T,C or G	
<400> 132	
acttttgcca ttttgtatataaaacaatc ttgggacatt ctcctgaaaa ctaggtgtcc	60
agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat	120
ctcaaattcc caaacagggg ctctgtgggaaaatgaggg aggacctttg tatctcggtt	180
tttagcaagt taaaatgaat atgacagggaa aggcttattt atcaacaaag agaagatgg	240
ggatgcttct aaaaaaaaaact ttggtagaga aaataggaat gctnaatcct agggaaagcct	300
gtaacaatct acaattggtc ca	322
<210> 133	
<211> 278	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(278)	
<223> n = A,T,C or G	
<400> 133	
acaaggccttc acaagttaa ctaaattggg attaatcttt ctgtantttt ctgcataatt	60
cttgggttttc ttccatctg gtcctgggt tgacaatttg tggaaacaaac tctattgtca	120
ctatttaaaaaaa aaaaatcacaa atctttccct ttaagctatg ttnaattcaa actattcctg	180
ctattcctgt ttgtcaaag aaattatatt ttcaaaaata tgtntatttg ttgtatgggt	240

cccacgaaac actaataaaaa accacagaga ccagcctg	278
<210> 134	
<211> 121	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(121)	
<223> n = A,T,C or G	
<400> 134	
gtttanaaaa cttgtttagc tccatagagg aaagaatgtt aaactttgta tttaaaaca	60
tgattctctg aggttaaact tggtttcaa atgttatttt tacttgtatt ttgctttgg	120
t	121
<210> 135	
<211> 350	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(350)	
<223> n = A,T,C or G	
<400> 135	
acttanaacc atgccttagca catcagaatc cctcaaagaa catcaagtata atcctataacc	60
atancaagtg gtgactgggt aagcgtagcga caaagggtcag ctggcacatt acttgtgtgc	120
aaacttgata cttttgttct aagttaggaac tagtatacag tncctaggan tggtaactcca	180
gggtcccccc caactcctgc agccgtcct ctgtgccagn ccctgnaagg aactttcgct	240
ccacctcaat caagccctgg gccatgtac ctgcaattgg ctgaacaac gtttgctgag	300
ttcccaagga tgcaaagcct ggtgctcaac tcctggggcgc tcaactcagt	350
<210> 136	
<211> 399	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(399)	
<223> n = A,T,C or G	
<400> 136	
tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga gcccagggtt	60
gctgtgattt tatccgataa ntccctgtga gaaaagataa tgagatgacg tgagcagcct	120
gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga	180
cctggccggcc agccagccag ccacaggtgg gcttcttcct tttgtggta caacnccaaag	240
aaaactgcag aggcccaggg tcaggtgtta gtgggtangt gaccataaaa caccaggtgc	300
tcccaggaac cccggccaaag gccatccccca cctacagccca gcatccccac tggcgtgatg	360
ggtgcagang gatgaagcag ccagntgttc tgctgtgg	399
<210> 137	
<211> 165	
<212> DNA	
<213> Homo sapien	

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<220>
<221> misc_feature
<222> (1)...(165)
<223> n = A,T,C or G

<400> 137
actgggtggtgg tngggggtga tgctgggttgtt anaagttgan gtgacttcan gatgggtgtgt      60
ggagggaaatgt tgtaacgtt gggatgtaga ngttttgccgtt gtcataaatg agcttcggga      120
ttggctggtc ccactgggtgg tcactgtcat tggtggggttt cctgt      165

<210> 138
<211> 338
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(338)
<223> n = A,T,C or G

<400> 138
actcaactgga atgccacatt cacaacagaa tcagagggtct gtgaaaacat taatggctcc      60
ttaactctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccac      120
tgctggcag tctccatgc ctccacagt gaaagggctt gagaaaaatc acatccaatg      180
tcatgtgttt ccagccacac caaaaggtgc ttgggtggaa gggctggggg catananggt      240
cangcctcag gaagcctcaa gttccattca gcttgcac tgcattcc ccatntttaa      300
aaaaactgt gcctttttt tttttttttaaaaattc      338

<210> 139
<211> 382
<212> DNA
<213> Homo sapien

<400> 139
ggaaatcttg gttttggca tctgggttgc ctatagccga ggccactttt acagaacaaa      60
gaaaggact tcagtaaga aggtgattt cagccagcct agtgcggaa gtgaaggaga      120
attcaaacat acctcgatcat tcctgggtgtt agcctggtcg gtcaccgccc tatcatctgc      180
atttgccta ctcaggtgct accggactct ggccccgtat gtctgttagtt tcacaggatg      240
ccttatttgtt ctctacacc ccacaggggcc ccctacttct tcggatgtgt ttttaataat      300
gtcagctatg tgcccatcc tcctcatgc cctccctccc tttcctacca ctgctgagtg      360
gcctggaaact tggtaaaatgt gt      382

<210> 140
<211> 200
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(200)
<223> n = A,T,C or G

<400> 140
accaaananctt cttctgttg tggatgttt tactataggg gtttngcttn ttctaaanat      60
acttttcatt taacancttt tggatgtt caggctgcac tttgctccat anaattattt      120
ttttcacatt tcaacttgta tggatgttc tcttanagca ttggtaaaat cacatattt      180
atattcagca taaaggagaa      200

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<210> 141
<211> 335
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(335)
<223> n = A,T,C or G

<400> 141
actttatTTT caaaacactc atatgttgcA aaaaacacat agaaaaataa agtttggTgg      60
gggtgcgtac taaacctca a gtcacagact ttatgtgac agattggagc agggtttgtt      120
atgcatgttag agaacccaaa ctaattttt aaacaggata gaaacaggct gtctgggtga      180
aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg      240
tttttctacc agttcagaga tnggttaatg actantcca atggggaaaa agcaagatgg      300
attcacaaac caagtaattt taaacaaaga cactt                                335

<210> 142
<211> 459
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(459)
<223> n = A,T,C or G

<400> 142
accaggtaa tattgccaca tatATCCTT ccaattgcgg gctaaacaga cgtgtattt      60
gggtgttta aagacaaccc agcttaatat caagagaaat tgtgacctt catggagtat      120
ctgatggaga aaacactgag tttgacaaa tcttattttt ttcagatagc agtctgatca      180
cacatggtcc aacaacactc aaataataaa tcaaataatna tcagatgtt aagattggc      240
ttcaaacatc atagccaatg atgcccgc tgcctataat ctctccgaca taaaaccaca      300
tcaacacctc agtggccacc aaaccattca gcacagttc cttaactgtg agctgtttga      360
agctaccagt ctgagcacta ttgactatnt tttcangct ctgaatagct cttagggatct      420
cagcangggg ggaggaacc agctcaacct tggcgtant                                459

<210> 143
<211> 140
<212> DNA
<213> Homo sapien

<400> 143
acatTTCTT ccaccaagtc aggactcctg gettctgtgg gagttcttat cacctgaggg      60
aaatccaaac agtctctctt agaaaggaat agtgcacca accccaccca tctccctgag      120
accatccgac ttccctgtgt                                140

<210> 144
<211> 164
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(164)
<223> n = A,T,C or G

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<400> 144
acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatctt gtcattttct      60
atctatacca ctctcccttc taaaaacaan aatcaactanc caatcaactta tacaatattg     120
aggcaattaa tccatatttg tttcaataa ggaaaaaaaag atgt                         164

<210> 145
<211> 303
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

<400> 145
acgttagacca tccaaaccttgc tatttgaat ggcaaacatc cagnagcaat tcctaaacaa      60
actggagggt atttataccca aattatccca ttcattaaca tgcccttc ctcaggctat      120
gcaggacagc tatacataagt cggcccaggc atccagatac taccatttgt ataaacttca      180
gttaggggagt ccatccaagt gacaggctta atcaaaggag gaaatggaac ataagccca      240
tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat      300
caa                                         303

<210> 146
<211> 327
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(327)
<223> n = A,T,C or G

<400> 146
actgcagctc aattagaagt ggtctctgac ttcatcanc ttctccctgg gctccatgac      60
actggccctgg agtgactcat tgctctgggtt ggtttagaga gtcctttgc caacaggccct      120
ccaagtctagg gctgggattt gttcccttcc cacattctag caacaatatg ctggccactt      180
cctgaacagg gaggggtggga ggagccagca tggacaaggc tgccacttgc taaaagttagcc      240
agacttgccc ctggccctgt cacacctact gatgaccccttgc tggccctgca ggatggaatg      300
taggggttag ctgtgtgact ctatgggt                                327

<210> 147
<211> 173
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(173)
<223> n = A,T,C or G

<400> 147
acattgttttt ttttagataa agcattgana gagctcttcc taacgtgaca caatggaagg      60
actggAACAC atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt      120
atattcaagg acatatgtta tatattatttc agttccatgt ttatagccctt gtt                         173

<210> 148

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<211> 477
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(477)
<223> n = A,T,C or G

<400> 148
acaaccacctt tatctcatcg aatttttaac ccaaactcac tcactgtgcc tttctatcct      60
atggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact      120
gcctactac ctgctgcaat aatcacattc ctttcctgtc ctgaccctga agccattggg      180
gtggcttag tgccatcg tccangcctg caccttgagc ctttgagctc cattgctcac      240
nccancccac ctcaccgacc ccattctt acacagctac ctccctgctc tctaaccac      300
tagattatnt ccaaatttag tcaattaagt tactattaac actctacccg acatgtccag      360
caccacttgtt aagcctctc cagccaacac acacacacac acacncacac acacacat      420
ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atggtgg      477

<210> 149
<211> 207
<212> DNA
<213> Homo sapien

<400> 149
acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggagaagac      60
taacgtattt tagagagcca aggaaggttt ctgtggggag tggatgtaa ggtggggcct      120
gatgataaat aagagtccgc caggttaagt ggtgggtgtgg tatggcaca gtgaagaaca      180
tttcaggcag aggaacacgc agtgaaa      207

<210> 150
<211> 111
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(111)
<223> n = A,T,C or G

<400> 150
accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatgg      60
cacttaatg tggcagtgt ttggacttgt taactantgg catcttggg t      111

<210> 151
<211> 196
<212> DNA
<213> Homo sapien

<400> 151
agcgcggcag gtcatttgc acattccaga tacctatcat tactcgatgc tggtgataac      60
agcaagatgg ctgttgcactc agggtcacca ccagctattt gaccttacta tgaaaaccat      120
ggataccaac cgaaaaaccc ctatccgc cagccccactg tggtccccac tgtctacgag      180
gtgcattccgg ctcatgt      196

<210> 152
<211> 132
<212> DNA

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<213> Homo sapien

<400> 152
 acagcacttt cacatgttaag aaggagaaaa ttccctaaatg taggagaaaatg ataaacagaac 60
 cttccccctt tcatacttagt gtggaaacct gatgtttat gttgacagga atagaaccag 120
 gagggagttt gt 132

<210> 153
 <211> 285
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(285)
 <223> n = A,T,C or G

<400> 153
 acaanaccca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag 60
 cttctgtct tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga 120
 gcacatcaat aaagtccaaa gtcttgact tggccttggc ttggaggaag tcatcaacac 180
 cctggctagt gagggtgcgg cgccgcctt ggtacgcgc atctgtgaag tcgtgcacca 240
 gtctgcaggc cctgtgaaag cgccgtccac acggagtnag gaatt 285

<210> 154
 <211> 333
 <212> DNA
 <213> Homo sapien

<400> 154
 accacagtcc ttttggccca gggcttcatg accctttctg tgaaaagcca tattatcacc 60
 accccaaatt tttccttaaa tatcttaac tgaaggggtc agcctttga ctgcaaagac 120
 ccttaagccgg ttacacagct aactcccact gcccctgatt tgtgaaatttgcctg 180
 attggcacag gagtcgaagg ttttgcgtc ccctcctccg tggAACGAGA ctctgatttgc 240
 agtttcacaa attctgggc cacctcgta ttgctcctctt gaaataaaat ccggagaatgt 300
 gtcaggcctg tctcatccat atggatcttc cgg 333

<210> 155
 <211> 308
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(308)
 <223> n = A,T,C or G

<400> 155
 actggaaata ataaaaccca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg 60
 gaaagtgttt tggaaactgt aaagtgccta acacatgate gatgatTTT gtataatat 120
 ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tggcccccag ccccagcccc 180
 atcacagctc actgctctgt tcatccaggc ccagcatgtt gttggcttattt cttttggct 240
 gcttttagcc tccanaagtt tctctgttgc caacccaaacc tctangtgtt aggcattgtt 300
 gcccctgggt 308

<210> 156
 <211> 295
 <212> DNA

<213> Homo sapien

<400> 156
accttgctcg gtgcttggaa catattagga actcaaaaata tgagatgata acagtgccta 60
ttattgatta ctgagagaac tgtagacat ttgttgaag attttctaca caggaactga 120
gaataggaga ttatgtttgg ccctcatatt ctctcctatc ctcctgcct cattctatgt 180
ctaatatatc ctaatcaaa taaggttagc ataatcagga aatcgaccaa ataccaat 240
aaaaccagat gtctatcctt aagatttca aatagaaaac aaattaacag actat 295

<210> 157
<211> 126
<212> DNA
<213> Homo sapien

<400> 157
acaagtttaa atagtgtgt cactgtgcgt gtgctgaaat gtgaaatcca ccacatttct 60
gaagagcaaa acaaattctg tcatgtatc tctatcttgg gtcgtggta tatctgtccc 120
cttagt 126

<210> 158
<211> 442
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (442)
<223> n = A,T,C or G

<400> 158
acccactggt ctggaaaca cccatcctta atacgatgat ttttctgtcg tgtaaaaatg 60
aanccagcg gctgccccta gtcagtcctt ccttccagag aaaaagagat ttgagaaaagt 120
gcctggtaa ttccaccatta atttcctccc ccaaactctc tgagtcttcc cttaatattt 180
ctgggtgttc tgaccaaagc aggtcatggt ttgtttagca ttggatcc cagtgaagta 240
natgttgta gccttgata cttagccctt cccacgcaca aacggagtgg cagagtgg 300
ccaaacctgt ttcccagtc cacgtagaca gattcacagt gcggattct ggaagctgga 360
nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg 420
tgttcattct ctgatgtcct gt 442

<210> 159
<211> 498
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (498)
<223> n = A,T,C or G

<400> 159
acttccaggtaacgttgg tttccgttga gcctgaactg atgggtgacg ttgttaggttc 60
tccaacaaga actgagggtt cagagcgggt agggaaaggt gctgtccag ttgcacctgg 120
gctgtgtgg actgttggt attcctcaact acggcccaag gttgtggaaac tggcanaaag 180
gtgtgtgtt gganttgagc tcggggggct gtggtaggtt gtgggtctt caacaggggc 240
tgctgtgtt ccgggangtg aangtgttgc gtcacttgag cttggccagc tctggaaagt 300
antanattct tcttgcaggc cagcgttgc ggagctggca ngggtcantg ttgtgtgtaa 360
cgaaccagtgc tgcgtgtgg tgggtgtana tcttccacaa agcctgaagt tatgggtgtcn 420
tcaggttana atgtggtttc agtgcctgtt ggcngctgtt gaaggttgc nattgtcacc 480

aagggaataa gctgtggt	498
<210> 160	
<211> 380	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(380)	
<223> n = A,T,C or G	
<400> 160	
acctgcatcc agcttcctg ccaaactcac aaggagacat caacctctag acagggaaac	60
agcttcagga tacttcagg agacagagcc accagcagca aaacaaatat tcccatgcct	120
ggagcatggc atagaggaag ctgaaaaatg tgggtctga ggaaggcatt tgagtctggc	180
cactagacat ctcatcagcc acttgtgtga agagatgcc catgacccca gatgcctctc	240
ccacccttac ctccatctca cacacttgag cttccactc tgtataattc taacatcctg	300
gagaaaaatg gcagttgac cgaacctgtt cacaacgta gaggctgatt tctaacgaaa	360
ctttagaat gaagcctgga	380
<210> 161	
<211> 114	
<212> DNA	
<213> Homo sapien	
<400> 161	
actccacatc ccctctgagc aggcggttgt cgttcaaggt gtatggcc ttgcctgtca	60
cactgtccac tggcccctta tccacttggt gcttaatccc tcgaaagagc atgt	114
<210> 162	
<211> 177	
<212> DNA	
<213> Homo sapien	
<400> 162	
actttctgaa tcgaatcaa tgatacttag tggatttta atatcctcat atatatcaa	60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagctt	120
tggtgatata taacttggca ataaccagt ctggtgatac ataaaactac tcactgt	177
<210> 163	
<211> 137	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(137)	
<223> n = A,T,C or G	
<400> 163	
catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccggtac	60
canagaaggc agtacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt	120
catcagcggc atgatgt	137
<210> 164	
<211> 469	
<212> DNA	

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(469)

<223> n = A,T,C or G

<400> 164

cttatcacaa tgaatgttct cctggcagc gttgtatct ttgccacatt cgtgacttta	60
tgcaatgcatt catgttatt catacctaatt gagggagttc caggagattc aaccaggaaa	120
tgcattgttca tcaaaggaaa caaacaccca ataaactcg agtggcagac tgacaactgt	180
gagacatgca cttgctacga aacagaattt tcatgttca cccttgttac tacacctgt	240
ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcg	300
gtggagaaga agacccaaa aaagacctgt tctgtcagt aatggataat ctaatgtct	360
tcttagtaggc acagggttc caggcaggc ctcatttcc tctggctt aatagtcaat	420
gattgtgttag ccatgcctat cagtaaaaag atntttgagc aaacacttt	469

<210> 165

<211> 195

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(195)

<223> n = A,T,C or G

<400> 165

acagttttt atanatatcg acattgccgg cacttgtgtt cagtttcata aagctggtgg	60
atccgcgttc attccactatt cttggcttag agtaaaaattt attcttatag cccatgtccc	120
tgcaggccgc ccggccgttag ttctcggttcc agtctgtttt gcacacaggg tgccaggact	180
tcctctgaga tgagt	195

<210> 166

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 166

acatcttagt agtgtggcac atcagggggc catcagggtc acagtcactc atagcctcgc	60
cgagggtcggat gttccacacca ccgggtttagg tgtgtcaat cttgggtttt ggcggccac	120
ttggagaagg gatatgtgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt	180
tttgcagacc agcctgagca agggggcgat gttcagtttcc agtccttct tcgtcagggt	240
gatgccaacc tcgtctangt tccgtggaa gctgggttcc acntcaccta caacctgggc	300
gangatctta taaagaggct ccnagataaa ctccacgaaa cttctctggg agctgttagt	360
nggggcctt ttggtaact ttc	383

<210> 167

<211> 247

<212> DNA

<213> Homo sapien

<220>

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<221> misc_feature
<222> (1)...(247)
<223> n = A,T,C or G

<400> 167
acagaggccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat      60
tggagcagaa actggagcaa gaagtggcc tggggctgaa gtagagacca aggccactgc      120
tatancata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac      180
tcaatctgan tccaaagtgg tggctggaac actggcatg acanaggcag tgactctgac      240
tgangtc      247

<210> 168
<211> 273
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(273)
<223> n = A,T,C or G

<400> 168
acttctaagt ttcttagaag tggaggatt gtantcatcc tgaaaatggg tttacttcaa      60
aatccctcan ccttgttctt cacnactgtc tatactgana gtgtcatgtt tccacaaagg      120
gctgacacct ggcctgnat tttactcat ccctgagaag cccttccag tagggtggc      180
aattcccaac ttccctgcca caagcttccc aggcttctc ccctgaaaa ctccagctt      240
agtcccagat acactcatgg gctgccctgg gca      273

<210> 169
<211> 431
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(431)
<223> n = A,T,C or G

<400> 169
acagccttgg ctccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc      60
agtcagacc agggtaaag gatgtgacat caacagttc tggttcaga acaggttcta      120
ctactgtcaa atgacccccc atacttcctc aaaggctgtg gtaagtttg cacaggtgag      180
ggcagcagaa aggggtant tactgatgga caccatttc tctgtatact ccacactgac      240
cttgcctatgg gcaaaggccc ctaccacaaa aacaatagga tcactgctgg gcaccagctc      300
acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaactgg      360
aaagtgatct gatactggat tcttaattac ctcaaaaagc ttctggggc catcagctgc      420
tcgaacactg a      431

<210> 170
<211> 266
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(266)
<223> n = A,T,C or G

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<400> 170
 acctgtggc tggctgtta tgcctgtgcc ggctgctgaa agggagttca gaggtggagc 60
 tcaaggagct ctgcaggcat tttgccaanc ctctccanag canagggagc aacctacact
 ccccgtaga aagacaccag attggagtcc tgggaggggg agttgggtg ggcatttgat 120
 gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct 180
 tcaaagctag gggctggca ggtgga 240
 266

<210> 171
 <211> 1248
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1248)
 <223> n = A,T,C or G

<400> 171
 ggcagccaaa tcataaacgg cgaggactgc agccgcact cgccgcctg gcaggcgcca 60
 ctggtcatgg aaaacgaatt gttctgctcg ggctgcctgg tgcatccgca gtgggtgctg 120
 tcagccgcac actgtttcca gaagttagt cagagctccat acaccatcggt gctggcctg 180
 cacagtcttgc aggcgcacca agagccaggg agccagatgg tggagggccag cctctccgt 240
 cgccacccag agtacaaacag acccttgcgc gctaaccgacc tcatgtcat caagttggac 300
 gaatccgtgt ccgagtcgtca caccatccgg agcatcagca ttgctcgca gtgccttacc 360
 gcggggact ctgcctcggt ttctggctgg ggtctgtgg cgaacggcag aatgcctacc 420
 gtgctgcagt ggtgtacgt gtcgggtggc tctgaggagg tctgcagtaa gctctatgac 480
 ccgctgtacc accccagcat gttctgcgc ggcggaggc aagaccagaa ggactcctgc 540
 aacgggtact ctggggggcc cctgatctgc aacgggtact tgcaggccct tttgtcttcc 600
 gaaaaagccc cgtgtggcca agttggcgtg ccaggtgtot acaccaacct ctgcaaattc 660
 actgagtgaa tagagaaaaac cgtccaggcc agttaactct gggactggg aaccatgaa 720
 attgaccccc aaatacatcc tgcggaaagga attcaggaat atctgttccc agcccccctc 780
 ccctcaggcc caggagtccca ggccccccagc ccctccccc tcaaaccac agtacagatc 840
 cccagccct cctccctcaag acccaggagt ccagacccccc cagccccc tccctcagac 900
 ccaggagtcc agcccccctc ccctcagacc caggagtccca gaccccccag cccctccccc 960
 ctcagaccca ggggtccagg ccccaacccc ctcccccctc agactcagag gtccaaagccc 1020
 ccaaccntc attccccaga cccagaggc caggcccag cccctcntcc ctcagaccca 1080
 gcggtccaat gccacctaga ctntccctgt acacagtgc cccctgtggc acgttgaccc 1140
 aaccttacca gttggtttt cattttngt cccttcccc tagatccaga aataaagttt 1200
 aagagaagng caaaaaaaaaaaaaaaa aaaaaaaaaaaa aaaaaaaaaaaa aaaaaaaaaa 1248

<210> 172
 <211> 159
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(159)
 <223> Xaa = Any Amino Acid

<400> 172
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
 1 5 10 15
 Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
 20 25 30
 Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
 35 40 45
 Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly

50	55	60
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu		
65	70	75
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe		80
85	90	95
Cys Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser		
100	105	110
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe		
115	120	125
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn		
130	135	140
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser		
145	150	155

<210> 173
<211> 1265
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(1265)
<223> n = A,T,C or G

<400> 173

ggcagccgc actcgagcc ctggcaggcg gcactggtca tggaaaacga attgttctgc	60
tccggcgatcc tggtgcatcc gcagtgggtg ctgtcagccg cacactgttt ccagaactcc	120
tacaccatcg ggctgggcct gcacagtctt gaggccgacc aagagccagg gagccagatg	180
gtggaggcca gcctctccgt acggcaccca gagtacaaca gacccttgcg cgctaacgac	240
ctcatgtca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc	300
attgcttcgc agtgcctac cgccggAAC tcttgcctcg tttctggctg gggctctgtcg	360
gcgaacgggtg agctcacggg tgtgtgtctg ccctcttcaa ggaggctctc tgcccagtctg	420
cgggggctga cccagagctc tgcgtcccag gcagaatgcc taccgtctg cagtgcgtga	480
acgtgtcggt ggtgtctgag gaggtctgca gtaagctcta tgaccctgt taccacccca	540
gcatgttctg cgccggcgga gggcaagacc agaaggactc ctgcaacgggt gactctgggg	600
ggccccctgat ctgcaacggg tacttgcagg gccttgcgtc tttcgaaaa gccccgtgtg	660
gccaagttgg cgtgccaggt gtctacacca acctctgcaa attcactgag tggatagaga	720
aaaccgtcca ggccagttaa ctctggggac tggaaaccca tggaaattgac ccccaaatac	780
atccctgcgga aggaattcag gaatatctgt tcccagcccc tcctccctca ggcccaggaa	840
tccagggccc cagccccctcc tccctcaaacc caagggtaca gatcccagc ccctcctccc	900
tcagacccag gagtccagac cccccagccc ctccctccctc agaccaggaa gtccagcccc	960
tcctccntca gaccaggag tccagacccc ccagccccctc ctccctcaga cccaggggtt	1020
gaggccccca accccctctc cttcagagtc agaggtccaa gcccccaacc cctcggtccc	1080
cagacccaga ggtnnagggtc ccagccccctc ttccntcaga cccagnggtc caatgccacc	1140
tagatTTCC ctgnacacag tggcccttgg tgnangttg acccaacctt accagttgg	1200
ttttcatTTT tngtccctt cccctagatc cagaaataaa gtttaagaga ngngcaaaaa	1260
aaaaaa	1265

<210> 174
<211> 1459
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(1459)
<223> n = A,T,C or G

<400> 174	
ggtcagccgc acactgtttc cagaagttag tgcatagact ctacaccatc gggctgggccc	60
tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg	120
tacggcaccc agagtacaac agacccttgc tgcataacga cctcatgctc atcaagttgg	180
acgaatccgt gtccgagtc gacaccatcc ggagcatcg cattgcttcg cagtgcctta	240
cccgccccaa ctottgcctc gtttctggct ggggtctgct ggcgaacggg gagctcacgg	300
gtgtgtgtct gccctttca aggaggctt ctgcccagtc gcgggggctg acccagagct	360
ctgcgttcca ggcagaatgc ctacgtgtct gcagtgcgtg aacgtgtcg gggtgtctga	420
ngaggtctgc antaagctct atgaccgcgt gtaccacccc ancatgttct gcgcggcgg	480
agggcaagac cagaaggact cctgcaacgt gagagagggg aaaggggagg gcaggcgact	540
cagggaaaggg tggagaaggg ggagacagag acacacaggg ccgcattggcg agatgcagag	600
atggagagac acacaggggg acagtgcacaa ctagagagag aaactgagag aacagagaaa	660
ataaacacacag gaataaaagag aagcaaagga agagagaaaac agaaacacac atgggggaggc	720
agaaacacac acacatagaa atgcagttga ctttccaaaca gcatggggcc tgagggcggt	780
gacctccacc caatagaaaa ttctcttata acttttgact ccccaaaaac ctgactagaa	840
atagcctact gttgacgggg agccttacca ataacataaa tagtcgattt atgcatacgt	900
tttatgcatt catgatatac ctttgttga attttttgtat atttctaagc tacacagttc	960
gtctgtgaat ttttttaaat ttttgcact ctccctaaaat ttttctgtat ttttttattga	1020
aaaaatccaa gtataagtgg acttgtcat tcaaaccagg gttgttcaag ggtcaactgt	1080
gtacccagag gaaaaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa	1140
aaatcaagac tctacaaaaga ggctggcag ggtggctcat gcctgttaatc ccagcacttt	1200
gggaggccag gcaggcagat cacttgaggt aaggagttca agaccagcct gcccaaaaatg	1260
gtgaaatcct gtctgtacta aaaataaaaaa agttagctgg atatgggtggc aggcgcctgt	1320
aatcccagct acttgggagg ctgaggcagg agaatttgctt gaatatggga ggcagagggtt	1380
gaagtggagtt gagatcacac cactataactc cagctggggc aacagagtaa gactctgtct	1440
aaaaaaaaaaaa aaaaaaaaaaa	1459

<210> 175
<211> 1167
<212> DNA
<213> *Homo sapien*

```
<220>
<221> misc_feature
<222> (1)...(1167)
<223> n = A,T,C or G
```

<400> 175

ggcgcaggccct	ggcaggcgcc	actggtcatg	gaaaacgaat	tgttctgtc	ggcgctctg	60
gtgcattccgc	agtgggtgct	gtcagccgca	cactgttcc	agaactcta	caccatcg	120
ctgggcctgc	acagtcttga	ggccgaccaa	gagccaggg	gccagatgg	ggaggcc	180
ctctccgtac	ggcacccaga	gtacaacaga	ctcttgctcg	ctaacgacct	catgctcatc	240
aagttggacg	aatccgtgtc	cgagtcgtac	accatccgga	gcatcagcat	tgcttcgcag	300
tgcccttaccg	cggggaaactc	ttgcctcgtn	tctggctggg	gtctgtggc	gaacggcaga	360
atgccttaccg	tgctgcactg	cgtgaacgtg	tcgggttgt	ctgaggangt	ctgcagtaag	420
ctctatgacc	cgtgttacca	ccccagcatg	ttctgcgcgg	gcccggggca	agaccagaag	480
gactcctgca	acgggtgactc	tggggggccc	ctgatctgca	acgggtactt	gcagggcc	540
gtgtctttcg	gaaaagcccc	gtgtggccaa	cttggcgtgc	caggtgtcta	caccaac	600
tgcaaattca	ctgagttggat	agagaaaaacc	gttccagncca	gttaactctg	ggacttggg	660
acccatgaaa	ttgaccccca	aatacactt	ggegaangaa	ttcaggaata	tctgttccca	720
gccccctcctc	cctcaggcccc	aggagtccag	gccccccagcc	cctcctccct	caaacc	780
gtacagatcc	ccagccccctc	ctccctcaga	cccaggagtc	cagacccccc	ageccctcnt	840
ccntcagacc	caggagtcca	gccccctcctc	cntcagacgc	aggagtccag	accccccagc	900
ccntcnccg	tcaagacccag	gggtgcaggc	ccccaaacccc	tntccntca	gagtca	960
tccaagcccc	caacccctcg	ttccccagac	ccagaggtnc	aggtcc	cgc	1020
tcagacccag	cggtccaatg	ccacctagan	tntccctgt	cacagtgc	cccttgtggc	1080
ngttgaccca	accttaccag	ttggtttcc	atttttgtc	ccttccccc	agatccagaa	1140
ataaaagtnta	agagaagcgc	aaaaaaaa				1167

<210> 176
<211> 205
<212> PRT
<213> Homo sapien

<220>
<221> VARIANT
<222> (1)...(205)
<223> Xaa = Any Amino Acid

<400> 176

Met	Glu	Asn	Glu	Leu	Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln	Trp
1				5					10				15		
Val	Leu	Ser	Ala	Ala	His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly	Leu
	20						25						30		
Gly	Leu	His	Ser	Leu	Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met	Val
	35						40					45			
Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Leu	Leu	Leu
	50						55				60				
Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu	Ser
	65						70				75			80	
Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala	Gly
							85				90			95	
Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg	Met
							100				105			110	
Pro	Thr	Val	Leu	His	Cys	Val	Asn	Val	Ser	Val	Val	Ser	Glu	Xaa	Val
							115				120			125	
Cys	Ser	Lys	Leu	Tyr	Asp	Pro	Leu	Tyr	His	Pro	Ser	Met	Phe	Cys	Ala
							130				135			140	
Gly	Gly	Gly	Gln	Asp	Gln	Lys	Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly	Gly
	145						150				155			160	
Pro	Leu	Ile	Cys	Asn	Gly	Tyr	Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly	Lys
							165				170			175	
Ala	Pro	Cys	Gly	Gln	Leu	Gly	Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu	Cys
							180				185			190	
Lys	Phe	Thr	Glu	Trp	Ile	Glu	Lys	Thr	Val	Gln	Xaa	Ser			
							195				200			205	

<210> 177
<211> 1119
<212> DNA
<213> Homo sapien

<400> 177

gcgcaactcgc	agccctggca	ggcggcactg	gtcatggaaa	acgaattgtt	ctgctcggtc	60
gtcctgggtc	atccgcagtg	ggtgctgtca	gccgcacact	gttccagaa	ctcctacacc	120
atcgggctgg	gcctgcacag	tcttgaggcc	gaccaagagc	caggagcca	gatgggtggag	180
gccagctct	ccgtacggca	cccagagttac	aacagaccct	tgctcgctaa	cgacctcatg	240
ctcateaagt	tggacgaatac	cgtgtccgag	tctgacaccca	tccggagcat	cagcattgtct	300
tgcgcgtgcc	ctaccgcggg	gaactcttgc	ctcggttctg	gctggggct	gctggcgaac	360
gatgtgtgt	ttgccccatcca	gtccccagact	gtggggaggct	gggagttgtga	gaagctttcc	420
caaccctggc	agggttgtac	catttcggca	acttccagtg	caaggacgtc	ctgtctgcattc	480
ctcaactgggt	gctcaactgca	tcaccggaa	cactgtgtac	aactagccag		540
caccatagtt	ctccgaagtc	agactatcat	gattactgtt	ttgactgtgc	tgtctattgt	600
actaaccatg	ccgatgttta	ggtgaattta	gcgtcaacttg	gcctcaacca	tcttggatcc	660
cagttatcct	cactgaattt	agatttcttg	cttcagtgac	agccattccc	acataatttc	720
tgcacccatag	agggtgaggga	tcatatagct	cttcaaggat	gctggacttc	ccctcacaaa	780

ttcatttctc ctgttgttagt	gaaaggcg	ccctctggag	cctcccagg	tgggtgtgc	840	
ggtcacaatg	atgaatgtat	gatcggttc	ccattacca	aagccttaa	atccctcatg	900
ctcagtagac	cagggcagg	ctagcatttc	ttcatttagt	gtatgtgc	cattcatgca	960
accacccatg	gactcctgga	ttctctgcct	agttgagctc	ctgcatgctg	cctccttggg	1020
gaggtgaggg	agagggccca	tggtaaatg	ggatctgtgc	agttgtaaaca	cattaggtgc	1080
ttaataaaca	gaagctgtga	tgttaaaaaaa	aaaaaaaaaa			1119

<210> 178
<211> 164
<212> PRT
<213> Homo sapien

<220>
<221> VARIANT
<222> (1) ... (164)
<223> Xaa = Any Amino Acid

Met	Glu	Asn	Glu	Leu	Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln	Trp
1				5					10						15
Val	Leu	Ser	Ala	Ala	His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly	Leu
									25						30
Gly	Leu	His	Ser	Leu	Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met	Val
								35	40						45
Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu	Leu
						50		55			60				
Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu	Ser
						65		70			75				80
Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala	Gly
							85			90					95
Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Asp	Ala	Val
						100		105			110				
Ile	Ala	Ile	Gln	Ser	Xaa	Thr	Val	Gly	Gly	Trp	Glu	Cys	Glu	Lys	Leu
						115		120			125				
Ser	Gln	Pro	Trp	Gln	Gly	Cys	Thr	Ile	Ser	Ala	Thr	Ser	Ser	Ala	Arg
						130		135			140				
Thr	Ser	Cys	Cys	Ile	Leu	Thr	Gly	Cys	Ser	Leu	Leu	Leu	Thr	Ala	Ser
						145		150			155				160
Pro	Gly	Thr	Leu												

<210> 179
<211> 250
<212> DNA
<213> Homo sapien

<400> 179

ctggagtgcc	ttgggtgtttc	aagccctgc	aggaagcaga	atgcaccc	tgaggcacct	60
ccagctgcc	ccggccgggg	gatgcggaggc	tcggagcacc	cttgcggc	tgtgattgt	120
gccaggcact	gttcatctca	gttttctgt	ccctttgctc	ccggcaagcg	cttctgctga	180
aagttcatat	ctggagcctg	atgtcttaac	gaataaagg	cccatgctcc	acccgaaaaaa	240
aaaaaaaaaa						250

<210> 180
<211> 202
<212> DNA
<213> Homo sapien

<400> 180
actagtcagg tgggtggaa ttccattgtg tggggccaa cacaatggct acctttaaca 60
tcacccagac cccgccccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta 120
ctctgctact cgaaaaactat ttttatgtaa ttaatgtatg ctttcttgg tataaatgcc 180
tgataaaaaa aaaaaaaaaa aa 202

<210> 181
<211> 558
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(558)
<223> n = A,T,C or G

<400> 181
tccytttgkt naggkkkg agacamccck agacctaann ctgtgtcaca gacttcyyngg 60
aatgtttagg cagtgcgt aatttcytcg taatgattct gtttattactt tcctnattct 120
ttattcctct ttcttctgaa gattaatgaa gtggaaaatt gaggtggata aataaaaaaa 180
ggtagtgtga tagtataagt atctaagtgc agatggaaagt gtgttatata tatccattca 240
aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaac 300
ctactctgtt ccttggctag aaaaaattat aacaggact ttgttagttt gggaaagccaa 360
attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw 420
tttattccc aggaatatgg kggtcatttt atgaatattt cscrggatag awgtwtgagt 480
aaaaycagtt ttggtaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc. 540
aaaaaaaaaa aaaaaaaaaa 558

<210> 182
<211> 479
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(479)
<223> n = A,T,C or G

<400> 182
acagggwttk grggatgcta agscccriga rwyggttga tccaaccctg gcttwtttc 60
agaggggaaa atggggccta gaagttacag mscatyttagy tggtgcgmtg gcacccctgg 120
cstcacacag astcccgagt agctgggact acaggcacac agtcaactgaa gcaggccctg 180
ttwgcaattc acgttgcac ctccaactta aacattcttc atatgtgatg tccttagtca 240
ctaaggttaa acttccac ccagaaaagg caacttagat aaaatcttag agtactttca 300
tactmttcta agtctcttc cagcctcaact kkgagtcctm cytgggggtt gataggaant 360
ntctcttggc ttctcaata aartctctat ycatctcatg tttatattgg tacgcatara 420
awtgstgara aaattaaaat gttctgggty mactttaaaa araaaaaaaaa aaaaaaaaaa 479

<210> 183
<211> 384
<212> DNA
<213> Homo sapien

<400> 183
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactgggcc 60
agtaccagta ccaataacag tgccagtgcc agtgcagca ccagtggtgg cttcagtgtct 120
ggtgcagcc tgaccgcccc tctcacattt ggctcttcg ctggccttgg tggagctgg 180
gccagcacca gtggcagctc tggcgtctgt ggttctcata acaagtgaga ttttagat 240

tgttaatcct gccagtcttt ctcttcaagc cagggtgcat cctcagaaac ctactcaaca	300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt	360
gccatttcaa aaaaaaaaaaaa aaaa	384
<210> 184	
<211> 496	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(496)	
<223> n = A,T,C or G	
<400> 184	
accgaattgg gaccgctggc ttataagcg tcatgttynt ccrgrtatkac ctcaacgagc	60
agggagatcg agtctatacg ctgaagaaat ttgaccgc gggacaacag acctgcttag	120
cccatccctgc tcggttctcc ccagatgaca aataactctsg acacccaatc accatcaaga	180
aacgcttcaa ggtgctcatg acccagcaac cgccgcctgt cctctgaggg tcccttaaac	240
tgtatgtcttt tctgccacct gttacccctc ggagactccg taacccaaact cttcggactg	300
tgagccctga tgcccttttg ccagccatac tctttggcat ccagtctctc gtggcgattt	360
attatgcttg tggaggcaat tcatgttgc atcacccata aaggaaacac atttgacttt	420
tttttcctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst	480
aaaaaaaaaaa aaaaaa	496
<210> 185	
<211> 384	
<212> DNA	
<213> Homo sapien	
<400> 185	
gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtgacttcc	60
caagtatcyt ggcgscggtc ttctaccgtc cctacctgca gatcttcggg cagattcccc	120
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct	180
gggcacaccc tcctggggcc caggcgggca cctgcgtctc ccagtatgcc aactggctgg	240
tggtgcgtct cctcgtcatac ttctctgtcg tggccaaacat cctgcgtggc aacttgctca	300
ttgcccattttt cagttacaca ttccggcaaaag tacaggcCAA cagcgatctc tactggaaag	360
gcccggcggtt accgcctcat ccgg	384
<210> 186	
<211> 577	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(577)	
<223> n = A,T,C or G	
<400> 186	
gagtttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctgc ttcataaccgc	60
tnccatcggtc atactgtagg ttgcacca cytcctggca tcttggggcg gcntaatatt	120
ccagggaaact ctcacatcaag tcaccgtcg taaaacctgt gggctgggttc tgccttcgc	180
tcggtgtgaa aggatctccc agaaggagtg ctgcgttcc cccacactt tggacttt	240
attgagtcga ttctgcgtgt ccagcaggag gtttaccag ctctctgaca gtggaggtcac	300
cagccctatc atgcgttgc mctgcggaa garcaccggag ccttgcgtgg gggkkgaagt	360
ctcaccggaa ttctgcattt ccagagagcc gtggcaaaag acattgacaa actcgccccag	420
gtggaaaaag amcamctctt ggargtgctn ggcgttcctc gtcmttggt ggcagcgctw	480

tcctttgac acacaaacaa gttaaaggca tttcagccc ccagaaantt gtcatcatcc	540
aagatntcgc acagcactna tccagttggg attaaat	577
<210> 187	
<211> 534	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(534)	
<223> n = A,T,C or G	
<400> 187	
aacatcttcc tgtataatgc tgtgttaatat cgatccgatn ttgtctgstg agaatycatw	60
actkgggaaaa gmaacattaa agcctggaca ctggattaa aattcacaat atgcaacact	120
ttaaacagtg tgtcaatctg ctccccynac ttgtcatca ccagtctggg akaagggtt	180
tgcccttattc acacctgtta aaagggcgct aagcattttt gattcaacat ctttttttt	240
gacacaagtc cgaaaaaaago aaaagtaaac agttatyaat ttgttagcca attcaacttc	300
ttcatgggac agagccatyt gattaaaaaa gcaaattgca taatattgag ctttygggagc	360
tgtatattga gcggaagagt agccttcta cttcaccaga cacaactccc tttcatattg	420
ggatgttnac naaagtwatg tctctwacag atggatgct tttgtggcaa ttctgttctg	480
aggatctccc agtttattta ccacttgac aagaaggcgt tttcttcctc aggc	534
<210> 188	
<211> 761	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(761)	
<223> n = A,T,C or G	
<400> 188	
agaaaaccagt atctctnaaa acaacctctc ataccttgc gacctaattt tgtgtgcgtg	60
tgtgtgtcg cgcatattat atagacaggc acatctttt tactttttaa aagcttatg	120
cctcttttgtt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct	180
ttgtcttctg tggaaatggg actagagaaa acacctatnt tatgagtcaa tctagttngt	240
tttattcgc atgaaggaaa ttccagatn acaacactna caaactctcc ctkgackarg	300
ggggacaaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa	360
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwktt wttctccctt	420
gcaaaaaaca tggatcngact tcccggtgag taatgccaag ttgtttttt tatnataaaaa	480
cttgccttc attacatgtt taaaagtggt gtggtgggcc aaaatattga aatgatggaa	540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgc	600
atgcttaatt cacaatgct aatttcatta taaatgtttg ctaaaataca ctttgaacta	660
tttttctgtt tcccccagagc tgagatntt gattttatgt agtatnaagt gaaaaantac	720
gaaaataata acattgaaga aaaananaaa aaanaaaaaaa a	761
<210> 189	
<211> 482	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(482)	
<223> n = A,T,C or G	

<400> 189
 tttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca 60
 caccggggct atnagaagca agaaggaaagg agggagggca cagcccttg ctgagcaaca 120
 aagccgcctg ctgccttc tcgtctgtc cttggcagg cacatggga gaccttccc 180
 aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt gcataagaag 240
 tgataggcac aggccacccg gtaacagaccc ctcggctcct gacaggtna ttgcgaccag 300
 gtcattgtgc cctgcccagg cacagctan atctggaaaaa gacagaatgc ttccctttc 360
 aaatttgct ngtcatngaa ngggcanttt tccaanttn gctnggtctt ggtacnctt 420
 gttcgccccca gtcenctc caaaaantat tcacccnnct ccnaattgct tgcnngnccc 480
 cc 482

<210> 190
 <211> 471
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(471)
 <223> n = A,T,C or G

<400> 190
 tttttttttt ttttaaaaca gttttcaca aaaaaattta ttagaagaat agtggtttg 60
 aaaactctcg catccagtga gaactaccat acaccacatt acagctngga atgtntcc 120
 aatgtcttgtt ccaaatacatac aatggAACCA ttcaatctt cacatgcacg aaagaacaag 180
 cgcttttgc atacaatgca caaaaaaaaaa aggggggggg gaccacatgg attaaaattt 240
 taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt 300
 tgaaaaattt catgtatgca atccaaccAA agaacttnat tggtgatcat gantntctta 360
 ctacatcnac ttgatcattt gccagaacn aaaagtttana ancacncngt aaaaaanana 420
 tctgtattn anttcaacctt ccgtacngaa aaatntnnnt tatacactcc c 471

<210> 191
 <211> 402
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(402)
 <223> n = A,T,C or G

<400> 191
 gagggattga aggtctgttc tastgtcggtt ctgttcagcc accaactcta acaagttgt 60
 gtcttcact cactgtctgt aagctttta acccagacwg tatcttcata aatagaacaa 120
 attcttcacc agtcacatct tctaggacct tttggattc agttgtata agctttcca 180
 ctcccttgc taagacttca tctggtaaag tcttaagtt tggtagaaagg aattyatgg 240
 ctctgtctct aacaatgtcc ttccttgaa gtatggctt gaacaaccca cctaaagtcc 300
 ctgtgtcat ccattttaaa tatacttaat agggcattgk tncacttaggt taaattctgc 360
 aagagtcatc tgtctgcaaa agttgcgtta gtatatctgc ca 402

<210> 192
 <211> 601
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature

<222> (1)...(601)
<223> n = A,T,C or G

<400> 192

gagctcgat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact	60
ggtctacccc acatgggagc agcatccgt agntatataa ggtcattccc tgagtcagac	120
atgcytyttt gaytaccgtg tgccaagtgc tggtgattct yaacacacyt ccattccgyt	180
ctttgtga aaaactggca ctktctgga actagcarga catcacttac aaattcacc	240
acgagacact taaaaggtgt aacaaagcga ytcttgatt gcttttgtc cctccggcac	300
cagttgtcaa tactaaccgg ctgggttgc ecacatcacat ttgtgatctg tagctctgga	360
tacatccct gacagtactg aagaacttct tctttgttt caaaagcara tcttgggtgcc	420
tgttggatca gttccatt tcccagtcyg aatgttcaca tggcatattt wacttccac	480
aaaacattgc gatttgaggg tcagcaacag caaatcctgt tccggcattg gctgcaagag	540
cctcgatgtc gccggccagc gccaaggcag gcccaccagc agcagaagca	600
g	601

<210> 193

<211> 608

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(608)

<223> n = A,T,C or G

<400> 193

atacagccca natccccacca cgaagatgcg ctgttgact gagaacctga tgcggtcact	60
ggtcccgctg tagccccagc gactctccac ctgctggaaag cggttgatgc tgactcytt	120
cccaacgcag gcagmagcgg gscggtaaa tgaactccay tcgtggctt gggtkgacgg	180
tkaaagtgcag gaagaggctg accacccgcg ggtccaccag gatgcccac tgcggggac	240
ctgcagcgaa actcctcgat ggtcatgagc ggaagcga tgaggcccag ggccttgc	300
agaaccccttcc gcctgttctc tggcgtcacc tgcaagctgt gccgctgaca ctcggcctcg	360
gaccagcggc caaacggcrt tgaacagccg cacccacgg atgcccagtg tgcgcgc	420
caggammgscc accagcgtgt ccaggtcaat gtcggtaag ccctccggg gtratggcgt	480
ctgcagtgtt ttgtcgatg ttctccaggc acaggctggc cagctgcgt tcatcgaaga	540
gtcgccctg cgtgagcgc atgaaggcgt tgcggctcg cagttttct tcaggaactc	600
cacgcaat	608

<210> 194

<211> 392

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 194

gaacggctgg accttgcctc gcattgtgtc tgctggcagg gaataccttgc aaggcagyt	60
ccagtccgag cagccccaga ccgctccgc ccgaagctaa gcctgcctct ggccctcccc	120
tccgcctcaa tgcagaacca gtagtggag cactgtgttt agagttaaaa gtgaacactg	180
tttgcattttt cttggaaatt tcctctgttata gttttttt cccatgtta atttccaaac	240
aacaacaaca aaataaacatg tttgcctgtt aagttgtata aaagttgtt attctgttatt	300
taaagaaaaat attactgtta cataactgc ttgcaatttc tgtatttatt gktntctstgg	360
aaataaaat agtattaaa ggttgtcant cc	392

<210> 195
 <211> 502
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(502)
 <223> n = A,T,C or G

<400> 195

ccsttkgagg ggtkaggkyc cagttccga	gtggaagaaa caggccagga	gaagtgcgtg	60
ccgagctgag gcagatgttc ccacagtgc	ccccagagcc stgggstata	gtytctgacc	120
cctcncaagg aaagaccacs ttctggggac	atgggctgga gggcaggacc	tagaggcacc	180
aagggaaaggc cccattccgg ggstgttccc	cgaggaggaa gggaaaggggc	tctgtgtgcc	240
ccccasaggc aagaggccct gagtcctggg	atcagacacc cttcacgtg	tatccccaca	300
caaatgcaag ctcaccaagg tcccctctca	gtcccccttcc stacaccctg	amcgccact	360
gscscacacc caccagc acgccaccccg	ccatgggar tgtgctcaag	gartgcng	420
gcarcgtgga catctngtcc cagaaggggg	cagaatctcc aatagangga	ctgarcmstt	480
gctnanaaaaa aaaaanaaaaaa aa			502

<210> 196
 <211> 665
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(665)
 <223> n = A,T,C or G

<400> 196

ggtaacttgg ttcatgtcc accacttagt	ggatgtcatt tagaaccatt	ttgtctgctc	60
cctcttggaaag ctttgcgcag agcggacttt	gtaattgtt gagaataact	gtgtattt	120
wagctgttk gagttgatts gcaccactgc	acccacaact tcaatatgaa	aacyawttga	180
actwatttat tatcttgtga aaagtataac	aatgaaaatt ttgttcatac	tgtattkac	240
aagtatgatg aaaagcaawa gatatataatt	cttttattat gttaaattat	gattgccatt	300
attaatcggc aaaatgtgga gtgtatgttc	ttttcacagt aatatatgcc	ttttgttaact	360
tcacttgggtt attttattgt aaatgartta	caaaattctt aatttaagar	aatggtatgt	420
watatttatt tcattaattt ctccctkgt	ttacgtwaat tttgaaaaga	wtgcatgatt	480
tcttgacaga aatcgatctt gatgtgtgg	aagtagttt acccacatcc	ctatgagtt	540
ttctttagaat gtataaagggt	tgtagccat cnaacttcaa	agaaaaaaat gaccacatac	600
tttgaatca ggctgaaatg tggcatgctn	ttctaattcc aactttataa	actagcaaann	660
aagtg			665

<210> 197
 <211> 492
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(492)
 <223> n = A,T,C or G

<400> 197

ttttntttttt ttttttttgc aggaaggatt	ccatttattt tggatgcatt	ttcacaaat	60
atgtttattt gagcgatcca ttatcagtga	aaagtatcaa gtgttataa	natttttagg	120

aaggcagatt cacagaacat gctngtcngc ttgcagttt acctcgtna gatnacagag	180
aattatagtc naaccagtaa acnaggaatt tactttcaa aagattaaat ccaaactgaa	240
caaaaatcta ccctgaaact tactccatcc aaatattgga ataanagtca gcagtgatac	300
attctcttct gaactttaga tttctagaa aaatatgtaa tagtgatcg gaagagctct	360
tgttcaaaag tacaacnaag caatgtccc ttaccatagg ccttaattca aactttgatc	420
catttcactc ccatcacggg agtcaatgct acctggaca cttgtatTTT gttcatnctg	480
ancntggctt aa	492
<210> 198	
<211> 478	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(478)	
<223> n = A,T,C or G	
<400> 198	
tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa	60
tgtntccacn acaaattcatn ttacntnagt aagaggccan ctacattgt aAACATACAC	120
ttagtatatt ttgaaaagga caagttaaa gtanacncat attgccanc atancacatt	180
tatacatggc ttgattgata ttttagcacag canaaactga gtgagttacc agaaanaaaat	240
natatatgtc aatcngattt aagataaaaa acagatccta tggtacatan catcntgtag	300
gagttgtggc tttatgtta ctgaaagtca atgcagttcc tgtacaaaaga gatggccgt	360
agcattcttag tacctctact ccatggtaa gaatcgtaa cttatgtta catatgtnc	420
gggttaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa	478
<210> 199	
<211> 482	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(482)	
<223> n = A,T,C or G	
<400> 199	
agtgacttgt cctccaacaa aacccttga tcaagttgt ggcactgaca atcagaccta	60
tgctagttcc tgcatactat tcgctactaa atgcagactg gaggggacca aaaaggggca	120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cgactttga	180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagttta	240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaaat aaagtcnaga	300
aaatttacct ggangaaaag aggcttngg ctggggacca tcccattgaa ccttctctta	360
anggacttta agaanaaaact accacatgtn tgnatcc tgggccnngg cggtttantg	420
aacntngacn ncaccctnt ggaatanant ctgacngcn tcctgaactt gtcctctgc	480
ga	482
<210> 200	
<211> 270	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(270)	
<223> n = A,T,C or G	

<400> 200
 cggccgcaag tgcaactcca gctggggccg tgcggaccaa gattctgcc a cagttggtc 60
 cgactgcgac gacggcgccg gcgcacagtgc cagggtcagc gcggggccct ggggtcttgc 120
 aaggctgac tgacccgc aaggctgtgt cacgtcccac gaccttgacg ccgtcgaaa 180
 cagccgaaac agagcccggt gaangcgaaa ggcctcgaaa agccctcgga aagggcgcc 240
 ccgagagata cgccggatcgca ggtggccgccc 270

<210> 201
 <211> 419
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(419)
 <223> n = A,T,C or G

<400> 201
 tttttttttt ttttggaaatc tactgcgagc acagcaggc agcaacaagt ttatggca 60
 gcttagcaagg taacagggtt gggcatggtt acatgttcaag gtcaacttcc tttgtcggtt 120
 ttgattgggt ttttttatg ggggggggtt ggggtagggg aaancgaagc anaantaaca 180
 tggagtggtt gcaaccctccc ttgtttttttt gttttttttt gttttttttt gttttttttt 240
 tctgtgaccg tttttttttt gacatcaatg ttattttttttt tcaggatatc tttttttttt 300
 tccactgtnt ctggaggggag attaggggtt cttttttttt tccaaanaaa atccacntga 360
 aaaatggaaatc tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 419

<210> 202
 <211> 509
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(509)
 <223> n = A,T,C or G

<400> 202
 tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60
 tggacttaa tccatttttt tttttttttt tttttttttt tttttttttt tttttttttt 120
 gtnattttnc aaaaatctaaa nnttatttcaa atntnagcca aantccttac ncaaatnnnaa 180
 tacncncaaaa aatcaaaaaat atacntntct ttccatccaaac ttngtttacat aataaaaaaa 240
 aatatatacg gctgggtttt tcaaaatgttcaattatcttcaatcactgcaaaac atntttttttt 300
 ggaactaaaaa taaaaaaaaa cactnccgca aagggtttttt ggaacaacaa atcnntttt 360
 caacancnnc nattataaaa atcatatctc aatctttagg ggaatataa cttcacacng 420
 ggatcttaac tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 480
 caatggaaatc nccnccnccncc tggacttagt 509

<210> 203
 <211> 583
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(583)
 <223> n = A,T,C or G

<400> 203

tttttttttt ttttttttga ccccccctttt ataaaaaaaca agttaccatt ttatTTact	60
tacacatatt tattttataa ttggatttag atattcaaaa ggcagctttt aaaatcaaac	120
taaatgaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt	180
gaaaatcttc tctagctttt ttgactgtaa atttttactt cttgtaaaac atccaaattc	240
atttttcttg tctttaaaat tatctaattctt tcccatTTTT tccctattcc aagtcaattt	300
gcttctctag cctcatttcc tagctttat ctactattag taagtggctt tttccttaaa	360
agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tatttctacc	420
tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tcctttatg	480
tccatttttag tcactaaacg atatcnaaaag tgccagaatg caaaaggTTT gtgaacattt	540
attcaaaagc taatataaga tatttccat actcatctt ctg	583

<210> 204
<211> 589
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(589)
<223> n = A,T,C or G

<400> 204

tttttttttnt tttttttttt ttttttnctc ttcttttttt ttganaatga ggatcgagtt	60
tttcaacttc tagatagggc atgaagaaaa ctcatctttc cagcttaaa ataacaatca	120
aatctcttat gctatcatat attttaagtt aaactaatga gtcactggct tatcttctcc	180
tgaagggaaat ctgttcattt ttctcattca tatagttata tcaagttacta ccttgcata	240
tgagaggTTT ttcttctcta tttacacata tatttccatg tgaatttgcata tcaaaccTTT	300
attttcatgc aaactagaaaa ataatgtntt ctttgcata agagaagaga acaatatnag	360
cattacaaaa ctgctcaaat tgTTTgttaa gnttattccat tataatttgcata tnggcaggag	420
ctaatacAAA tcacatttac ngacnacaa taataaaaact gaagtaccag ttaaatatcc	480
aaaataattt aaggaacatt ttagctgg gtataatttgcata ttaatttgcata ttacaagcat	540
ttattnagaa tgaatttgcata tgTTTattt ccntagccca acacaatgg	589

<210> 205
<211> 545
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(545)
<223> n = A,T,C or G

<400> 205

tttttntttt ttttttcaatc aataatcaga acaatatttta tttttatattt taaaattcat	60
agaaaaagtgc cttacatttta ataaaaagtttt gtttctcaaa gtgatcagag gaatttagata	120
tngtcttgaa caccaatattt aatttgagga aaatacaccat aatacatttta agtaaatttt	180
ttaagatcat agagcttgta agtggaaaaga taaaatttgcata cttcagaaac totgagcatt	240
aaaaatccac tatttgcata taaaatttacta tgactttttt gctttatattt tttgtatgaat	300
atgggggtgtc actggtaaac caacacatttca tgaaggatc attacttgcata gatagattct	360
tatgtactttt gctanatnac gtggatatga gttgacaatg ttcttcttct tcaatctttt	420
aaggggcnga ngaaatgagg aagaaaagaa aaggatttgcata ctttgcata tttctatnng	480
aaggatttgcata ttttttttttgcata ttttttttttgcata ttttttttttgcata ttttttttttgcata	540
aaccc	545

<210> 206
<211> 487

<212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(487)
 <223> n = A,T,C or G

<400> 206

tttttttttt	tttttagtc	aagtttctna	tttttattat	aattaaagtc	ttggtcattt	60
catttattag	cctgcact	tacatattta	aattaaagaa	acgttnttag	acaactgtta	120
caatttataa	atgtaagggt	ccattattga	gtanatataat	tcctccaaga	gtggatgtgt	180
cccttcetccc	accaactaat	gaancagcaa	cattagtttta	attttatttag	tagatnatac	240
actgctgcaa	acgctaattc	tcttcctcat	ccccatgtng	atatttgtta	tatgtgtgag	300
ttggtnagaa	tgcatacana	atctnacaat	caacagcaag	atgaagctag	gcntgggctt	360
tcggtgaaaa	tagactgtgt	ctgtctgaat	caaatgatct	gacctatcct	cggtggcaag	420
aactcttcga	accgcttcct	caaaggcngc	tgccacattt	gtggcntctn	ttgcacttgt	480
ttcaaaa						487

<210> 207
 <211> 332
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(332)
 <223> n = A,T,C or G

<400> 207

tgaattggct	aaaagactgc	attttanaa	ctagcaactc	ttatttcctt	cctttaaaaaa	60
tacatagcat	taaatcccaa	atcctattta	aagacctgac	agcttggagaa	ggtcaactact	120
gcatttatag	gaccctctgg	tggttctgct	gttacntttg	aantctgaca	atccttgana	180
atctttgcat	gcagaggagg	taaaaggat	tggattttca	cagaggaana	acacagcgca	240
gaaaatgaagg	ggccaggcgtt	actgagcttg	tccactggag	ggctcatggg	tgggacatgg	300
aaaagaaggc	agcctaggcc	ctggggagcc	ca			332

<210> 208
 <211> 524
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(524)
 <223> n = A,T,C or G

<400> 208

agggcgtgg	gccccggggcg	ttactgtttt	gtctcagtaa	caataaatac	aaaaagactg	60
gttgtgttcc	ggccccatcc	aaccacgaag	ttgatttctc	ttgtgtgcag	agtgaactgat	120
tttaaaggac	atggagctt	tcacaatgtc	acaatgtcac	agtgtgaagg	gcacactcac	180
tcccgcgtga	ttcacattta	gcaaccaaca	atagctcatg	agtccataact	tgtaaatact	240
tttggcagaa	tacttnttga	aacttgcaga	tgataactaa	gatccaagat	atttcccaa	300
gtaaatagaa	gtgggtcata	atattaatta	cctgttcaca	tcagcttcca	tttacaagtc	360
atgagcccgag	acactgacat	caaactaagc	ccacttagac	tcctcaccac	cagtctgtcc	420
tgtcatcaga	caggaggctg	tcaccttgac	caaattctca	ccagtcatac	atctatccaa	480
aaaccattac	ctgatccact	tccggtaatg	caccacccctg	gtga		524

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<210> 209
<211> 159
<212> DNA
<213> Homo sapien

<400> 209
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg      60
tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca      120
caaaggactc tcgacccaa ctgccccaga ccctctcca      159

<210> 210
<211> 256
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(256)
<223> n = A,T,C or G

<400> 210
actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttgc ttgaactgcc      60
actgaatttc tttccacttg gactattaca tgccanttg gggactaatg gaaaaacgta      120
tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat      180
ttgcagggtg naaatgggan ggctggtttgc ttanatgaac agggacatag gaggtaggca      240
ccaggatgct aaatca      256

<210> 211
<211> 264
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(264)
<223> n = A,T,C or G

<400> 211
acattgtttt tttgagataa agcattgaga gagctctcct taacgtgaca caatggagg      60
actggAACAC atacccacat ctttgttctg aggataatt ttctgataaa gtcttgctgt      120
atattcaAGC acatatgttA tatattattc agttccatgt ttatagccta gttaaggaga      180
ggggagatac attcngaaag aggactgaaa gaaatactca agtngggaaaa cagaaaaaga      240
aaaaaaggag caaatgagaa gcct      264

<210> 212
<211> 328
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

<400> 212
acccaaaaat ccaatgctga atatggct tcattattcc canattctt gattgtcaaa      60
ggatTTAATG ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag      120
gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgccccccag      180

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ttnaatttca ttcccattga cttggatcc ttatcatcg ccagagagat tgaaaattta	240
ccccctacnac tctttactct ctgganaggg ccagtggtgg tagctataag cttggccaca	300
tttttttttc ctttattcct ttgtcaga	328
<210> 213	
<211> 250	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(250)	
<223> n = A,T,C or G	
<400> 213	
acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagg	60
taaagcattg ctcactgaag ggtatagaatg gactgccagg agggaaagta agccaaggct	120
cattatgcca aaggnatata acatttcaat tctccaaact tcttcctcat tccaagagtt	180
ttcaatattt gcatgaacct gctgataanc catgttaana aacaatatac tctctnacct	240
tctcatcggt	250
<210> 214	
<211> 444	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(444)	
<223> n = A,T,C or G	
<400> 214	
acccagaatc caatgctgaa tatttggctt cattattccc agatttttg attgtcaaag	60
gatTTaatgt tgtctcagct tggcacttc agttaggacc taaggatgcc agccggcagg	120
tttatatatg cagcaacaat attcaagcgc gacaacaggt tattgaactt gcccggcagt	180
tgaatttcat tcccattgac ttggatcct tatcatcagg canagagatt gaaaatttac	240
ccctacgact ctttactctc tggagagggc cagtgggtgg agctataagc ttggccacat	300
tttttttcc ttatttcctt tgtcagagat gcgattcatc catatgctan aaaccaacag	360
agtgactttt aaaaaattcc tataganatt gtgaataaaa ctttacctat agttgccatt	420
actttgtctt ccctaataata cctc	444
<210> 215	
<211> 366	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(366)	
<223> n = A,T,C or G	
<400> 215	
acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagg	60
taaagcattg ctcactgaag ggtatagaatg gactgccagg agggaaagta agccaaggct	120
cattatgcca aaggnatata acatttcaat tctccaaact tcttcctcat tccaagagtt	180
ttcaatattt gcatgaacct gctgataagc catgttgaga aacaatatac tctctgacct	240
tctcatcggt aaggcagagggc tggtaggcaac atggaccata gcgaanaaaa aacttagtaa	300
tccaagctgt tttctacact gtaaccaggt ttccaaccaa ggtggaaatc tcctataactt	360

gggcc

366

<210> 216			
<211> 260			
<212> DNA			
<213> Homo sapien			
<220>			
<221> misc_feature			
<222> (1)...(260)			
<223> n = A,T,C or G			
<400> 216			
ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc	60		
caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctntnc atttttttat	120		
taataaaaag tnnaaaaaggc ctcttccaa ctttttccc ttnggctgga aaatttaaaa	180		
atcaaaaaatt tcctnaagtt ntcaagctat catatatact ntatcctgaa aaagcaacat	240		
aattcttcct tccctcctt	260		
<210> 217			
<211> 262			
<212> DNA			
<213> Homo sapien			
<220>			
<221> misc_feature			
<222> (1)...(262)			
<223> n = A,T,C or G			
<400> 217			
acctacgtgg gtaagttan aaatgttata atttcagggaa naggaacgca tataattgtat	60		
tcttgccatat aattttctat ttaataagg aaatagcaaa ttgggggtggg gggaatgttag	120		
ggcattctac agttttagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt	180		
atgaataatc tgtatgatta tatgtctcta gacttagattt ataattagcc acttacccta	240		
atatccttca tgcttgtaaa gt	262		
<210> 218			
<211> 205			
<212> DNA			
<213> Homo sapien			
<220>			
<221> misc_feature			
<222> (1)...(205)			
<223> n = A,T,C or G			
<400> 218			
accaagggtgg tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca	60		
ccccctatcaa ctccccttttgg tagtaaactt ggaaccttgg aaatgaccag gccaaagactc	120		
aggccctcccc agttctactg acctttgtcc ttangtnna ngtccagggt tgcttagaaa	180		
anaaaatcagc agacacaggt gtaaa	205		
<210> 219			
<211> 114			
<212> DNA			
<213> Homo sapien			
<400> 219			

tactgttttg tctcagtaac aataaaataca aaaagactgg ttgtgttccg gccccatcca	60
accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga	114
<210> 220	
<211> 93	
<212> DNA	
<213> Homo sapien	
<400> 220	
actagccagc acaaaggca gggtagcctg aattgcttc tgctcttac atttcttta	60
aaataagcat ttagtgctca gtccctactg agt	93
<210> 221	
<211> 167	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(167)	
<223> n = A,T,C or G	
<400> 221	
actangtgca ggtgcgcaca aatatttgc gatattccct tcatcttgc ttccatgagg	60
tctttgccc agcctgtggc tctactgttag taagttctg ctgatgagga gccagnatgc	120
cccccaactac cttccctgac gctcccccana aatcacccaa cctctgt	167
<210> 222	
<211> 351	
<212> DNA	
<213> Homo sapien	
<400> 222	
agggcggtggt gcgaggggcg gtactgacct cattagtagg aggtgcatt ctggcacccc	60
gttcttcacc tgcctcccaa tcctaaaag gcccatactgc ataaagtcaa caacagataa	120
atgtttgtctg aattaaagga tggatgaaaa aaattaataa tgaatttttgc cataatccaa	180
ttttctcttt tatatttcta gaagaagttt cttgagcct attagatccc gggaatctt	240
taggtgagca tgatttagaga gctttaggt tgcttttaca tatatctggc atatttgagt	300
ctcgatcaa aacaatagat tggtaaaggt ggtattatttgc tattgataag t	351
<210> 223	
<211> 383	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(383)	
<223> n = A,T,C or G	
<400> 223	
aaaacaaaca aaaaaaaaaa acaatttttc attcagaaaa attatcttag ggactgatat	60
tggtaattat ggtcaattta atwrtrttkt gggcatttc cttacattgt ctgtacaaga	120
ttaaaatgtc tggccaaaa ttgttgcattt tatttggaga cttcttatca aaagtaatgc	180
tgc当地ggaa agtctaagga atttagtagtgc ttcccmmtcac ttgtttggag tggctattc	240
taaaagattt tgatttgcattt gaatgacaat tatattttaa ctttgggggg gggaaanagt	300
ataggaccac agtcttactt tctgatactt gtaaattaat ctttattgc acttgttttgc	360
accattaaggc tatatgttta aaa	383

<210> 224
 <211> 320
 <212> DNA
 <213> Homo sapien

<400> 224

cccctgaagg cttcttgtta gaaaatagta cagttacaac caataggaac aacaaaaaga
 aaaagttgt gacattgttag tagggagtgt gtacccctta ctccccatca aaaaaaaaaat
 ggatacatgg ttaaaggata raaggcata attttatcat atgttctaaa agagaaggaa
 gagaaaatac tactttctcr aaatggaagc ccttaaaggt gcttgatac tgaaggacac
 aaatgtggcc gtccatcctc ctтарагт gcatgacttg gacacggtaa ctgttgacагт
 ттарактcm gcattgtgac

<210> 225
 <211> 1214
 <212> DNA
 <213> Homo sapien

<400> 225

gaggactgca gccgcactc gcagccctgg caggcggcac tggtcatgga aaacgaattt
 ttctgctcg gggtcctggt gcatccgcag tgggtctgt cagccgcaca ctgttccag
 aactcctaca ccatcgggct gggcctgcac agtcttgagg ccgaccaga gccaggagc
 cagatggtgg agggcagcct ctccgtacgg caccaggat acaacagacc ctgctcgct
 aacgacctca tgctcatcaa gttggacgaa tccgtctcg agtctgacac catccggagc
 atcagcattg ctgcgtcg ggaactctt gcctcggtc tgctgggt
 ctgctggcga acggcagaat gcctaccgtg ctgcgtcg tgaacgtgtc gttgggtgtct
 gaggaggct gcagtaagct ctatgacccg ctgtaccacc ccagcatgtt ctgcggccgc
 ggaggccaag accagaagga ctccgtcaac ggtgactctg gggggccct gatctgcaac
 gggtaattgc agggcctgt gtcttcgga aaagccccgt gtggccaaatg tggcgtgcca
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 taactctgg gactggaaac ccatgaaatt gaccccaaa tacatctgc ggaaggaatt
 caggaatatc tggcccagc ccctccccc tcaggcccag gagtccagge ccccagcccc
 tcctccctca aaccaagggt acagatcccc agccctctt ccctcagacc caggagtcca
 gaccccccag ccctccctcc ctcagaccca ggagtccagc ccctccccc tcagacccag
 gagtccagac ccccaagccc ctccctcc cagaccagggt gtccaggccc ccaacccctc
 ctccctcaga ctcagaggc caagccccca accccctctt ccccaagaccc agaggtccag
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 cagtggccccc ttgtggcagc ttgaccaac ctaccagtt gttttcat ttttgtccc
 ttcccttag atccagaaat aaagtctaag agaagcgc当地 aaaaaaaaaa aaaaaaaaaa
 aaaaaaaaaa aaaa

<210> 226
 <211> 119
 <212> DNA
 <213> Homo sapien

<400> 226

acccagtagtgc tgcagggaga cgaaacccca tgtgacagcc cactccacca ggttcccaa
 agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcagc ataaccagt

<210> 227
 <211> 818
 <212> DNA
 <213> Homo sapien

<400> 227

acaattcata gggacgacca atgaggacag ggaatgaacc cggctctccc ccagccctga

tttttgctac atatgggtc cttttcatt ctttgcaaaa acactgggtt ttctgagaac	120
acggacggtt cttagcacaa tttgtaaaat ctgtgtaraa ccgggcttgc caggggagat	180
aattttccctc ctctggagga aagggtgtga ttgacaggca gggagacagt gacaaggcta	240
gagaagcca cgctcgccct tctctgaacc aggtatggac ggcagacccc tgaaaacgaa	300
gcttgccttc ttccaatcag ccacttctga gaacccccc ctaacttcct actggaaaag	360
agggctctc caggagcagt ccaagagttt tcaaagataa cgtgacaact accatctaga	420
ggaaagggtg caccctcagc agagaagccg agagcttaac tctggtcgtt tccagagaca	480
acctgctggc tgcgtgggta tgcccccacg ctttgagagg ccactacccc atgaacttct	540
gccatccact ggacatgaag ctgaggacac tgggcttcaa cactgagttg tcatgagagg	600
gacagctct gcctcaagc cggtcgaggc cagcaaccac tctccccc tttctcacgc	660
aaagccatc ccacaaatcc agaccatacc atgaagcaac gagacccaaa cagttggct	720
caagaggata tgaggactgt ctccgtgg ctttggctg acaccatgca cacacacaag	780
gtccacttct aggtttcag cctagatggg agtcgtgt	818

<210> 228
<211> 744
<212> DNA
<213> Homo sapien

<400> 228	
actggagaca ctgttgaact tgatcaagac ccagaccacc ccaggtctcc ttcgtggat	60
gtcatgacgt ttgacataacc tttggAACGA gcctccctct tgaaagatgg aagaccgtgt	120
tcgtggccga cctggcctct cctggcctgt ttcttaagat gcgaggatcac atttcaatgg	180
taggaaaagt ggcttcgtaa aatagaagag cagtcaactgt ggaactacca aatggcgaga	240
tgctcggtgc acattggggat gctttggat aaaagattt tgagccaact attctctggc	300
accagattct aggccagttt gttccactga agctttccc acagcagtcc acctctgcag	360
gctggcagct gaatggcttg cccggggctc tggcaaga tcacactgag atcgatgggt	420
gagaaggcta ggtatgtttt ctatgtttct tagctgtcac gttggctct tccagggttgg	480
ccagacgggtt tggccactc ctttcaaaa cacaggcgcc ctccctgtga cagtgaccgg	540
ccgtggatgc ctttggccca ttccagcagt cccagttatg catttcaagt ttggggtttg	600
ttcttttgtt taatgttccct ctgtgttgc agctgttttc atttctctgg ctaaggcagoa	660
ttgggagatg tggaccagag atccactct taagaaccag tggcggaaaga cactttcttt	720
cttcactctg aagtagctgg tggt	744

<210> 229
<211> 300
<212> DNA
<213> Homo sapien

<400> 229	
cgagtctggg tttgtctat aaagtttgc ccctcccttt ctcatccaaa tcatgtgaac	60
cattacacat cggaaataaaaa gaaagggtggc agacttgcac aacgccaggc tgacatgtgc	120
tgcagggtt tttttttta attattattt ttagaaacgt caccacagt ccctgttaat	180
ttgtatgtga cagccaaactc tgagaagggtc ctatccccc acctgcagag gatccagtct	240
cactaggctc ctccctggcc tcacactgga gtctccggca gtgtgggtgc ccactgacat	300

<210> 230
<211> 301
<212> DNA
<213> Homo sapien

<400> 230	
cagcagaaca aatacacaata tgaagagtgc aaagatctca taaaatctat gctgaggaat	60
gagcgacagt tcaaggagga gaagctgca gagcagctca agcaagctga ggagctcagg	120
caatataaaag tcctgggtca cactcaggaa cgagagctga cccagttaa ggagaaggttg	180
cgggaaaggga gagatgcctc cctctcattt aatgagcato tccaggccct cctcactccg	240
gatgaaccgg acaagtccccca gggcaggac ctccaaagaaa cagacctcgccgcaccac	300
g	301

<210> 231
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 231
 gcaagcacgc tggcaaatct ctgtcaggc agctccagag aagccattag tcatttttagc 60
 caggaactcc aagtccacat ccttggcaac tggggacttg cgccaggtag ccttgaggat 120
 ggcaacacgg gacttctcat caggaagtgg gatgttagatg agctgatcaa gacggccagg 180
 tctgaggatg gcaggatcaa tgatgtcagg ccggttggta ccgccaatga tgaacacatt 240
 ttttttgtg gacatgccat ccatttctgt caggatctgg ttgatgactc ggtcagcagc 300
 c 301

<210> 232
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 232
 agtaggtatt tcgtgagaag ttcaacacca aaactggAAC atagttctcc ttcaagtgtt 60
 ggcgacagcg gggcttcctg attctggaaataactttgt gtaaattaac agccacctat 120
 agaagagtcc atctgctgtg aaggagagac agagaactct gggtccgTC gtcctgtcca 180
 cgtgctgtac caagtgcTgg tgccagcctg ttacctgttc tcactgaaaa tctggctaatt 240
 gctcttgtt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300
 g 301

<210> 233
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 233
 atgactgact tcccagtaag gctctctaag ggtaagtag gaggatccac aggatttgag 60
 atgctaaggc cccagagatc gtttgcattca acccttttat tttcagaggg gaaaatgggg 120
 cctagaagtt acagagatc tagctgtgc gctggcaccC ctggcctcac acagactccc 180
 gagtagctgg gactacaggc acacagtac tgaagcaggg cctgttagca attctatgcg 240
 tacaaattaa catgagatga gttagagactt tattgagaaa gcaagagaaa atcctatcaa 300
 c 301

<210> 234
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 234
 aggtcctaca catcgagact catccatgat tgatatgaat ttaaaaatta caagcaaaga 60
 cattttattc atcatgatgc tttctttgt ttcttctttt cgttttttc tttttttttt 120
 tcaatttcag caacatactt ctcaatttct tcaggattta aaatctttag ggatttgatct 180
 cgcctcatga cagcaagtgc aatgttttg ccacctgact gaaccacttc caggagtgc 240
 ttgatcacca gcttaatggt cagatcatct gcttcaatgg ctgcgtcagt atagtttttc 300
 t 301

<210> 235
 <211> 283
 <212> DNA
 <213> Homo sapien

<400> 235
tggggctgtg cataggcgg gttttagaaaa tattcaattc tcagcagaag ccagaatttg 60
aattccctca tcttttaggg aatcattac caggtttgc gaggattcg acagctcagg 120
tgcttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaaata 180
atgttatctt tgaactgtatc ctcataggag agaatataag aactctgagt gatatcaaca 240
ttaggattc aaagaaaat tagatcca ctcacactgg tca 283

<210> 236
<211> 301
<212> DNA
<213> Homo sapien

<400> 236
aggtcctcca ccaactgcct gaagcacggtaaaaattggg aagaagtata gtgcagcata 60
aatactttta aatcgatcg atttccctaa cccacatgca atcttctca ccagaagagg 120
tcggagcagc atcattaata ccaaggcagaa tgcgtatag ataaatacaa tggtatatag 180
tggtagacg gcttcatgag tacagtgtac tgggtatcg taatctggac ttgggttgt 240
aagcatcgtg taccagtcg aaagcatcaa tactcgacat gaacgaatat aaagaacacc 300
a 301

<210> 237
<211> 301
<212> DNA
<213> Homo sapien

<400> 237
cagtggtagt gggtgggac gtggcggtgg tctgtggcctttttggc cccgtcaca 60
actcaatttt ttttcgtcc tttttggcct tttccaattt gtccatctca attttctggg 120
ccttggctaa tgcctcatag taggatcct cagaccagcc atggggatca aacatatcct 180
ttggtagtt ggtgccaagc tctgtcaatgg cacagaatgg atcagcttct cgtaaaatcta 240
gggttccgaa attttttctt cttttggata atgttagttca tatccattcc ctcccttata 300
t 301

<210> 238
<211> 301
<212> DNA
<213> Homo sapien

<400> 238
ggcaggttt tttttttttt ttttttggatgtgcagaccc ttgttttatttgtctgactt 60
gttcacagtt cagccccctg ctcagaaaac caacgggcca gctaaggaga ggaggaggca 120
ccttggagact tccggagtcg aggctctcca gggttccccca gcccattcaat cattttctgc 180
acccctgccc tggaagcag ctccctgggg ggtggaaatg ggtgactaga agggatttca 240
gtgtgggacc cagggtctgt tcttcacagt aggaggtggaa agggatgact aattttttta 300
t 301

<210> 239
<211> 239
<212> DNA
<213> Homo sapien

<400> 239
ataaggcagct agggattct ttatggatgtatgtcctaataaaagtcc acataactgc 60
ttctgtcaaa ccatgataact gagcttgcg acaacccaga aataactaag agaaggcaaa 120
cataataacct tagagatcaa gaaacatttacatgttacatgttataaa atagctcaac 180
attcagccag tgtagtagatgtgatgtcgcatacagatgttacatgttacatgttataaa 239

<210> 240

<211> 300
 <212> DNA
 <213> Homo sapien

<400> 240
 ggtcctaatt aagcagcagc ttccacattt taacgcagg ttaacggtgat actgtccttt 60
 gggatctgcc ctccagtgg aaccttttaag gaagaagtgg gcccagact agttccacat 120
 gctgggtgag ccagatgact tctgttcctt ggtcaacttcc ttcaatgggg cgaatgggg 180
 ctgccagggtt ttaaaatca tgcttcatct tgaagcacac ggtcaacttca ccctcctcac 240
 gctgtgggtg tactttgatg aaaataccca ctttggc ctttctgaag ctataatgtc 300

<210> 241
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 241
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 cctcttggaa gaaaactcca gcagctatgt tggtgtctct gaggaaatgc aacaaggctg 120
 ctcctccatg tattggaaaa ctgcaaactg gactcaactg gaaggaagtg ctgctgccag 180
 tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtctttct 240
 tcctcctcct gtcatacggt ctctctcaag catcctttgt tgcaggggc ctaaaaggga 300
 g 301

<210> 242
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 242
 ccgaggtcct gggatgcaac caatcactct gttcacgtg acttttatca ccatacaatt 60
 tgtggcattt cctcattttc tacattttag aatcaagagt gtaaataaat gtatatcgat 120
 gtcttcaaga atatatcatt ccttttcac tagaaccat tcaaaatata agtcaagaat 180
 cttaatatca acaaataatat caagcaaact ggaaggcaga ataactacca taattttagta 240
 taagtaccca aagttttata aatcaaaagc cctaattgata accatttttta gaattcaatc 300
 a 301

<210> 243
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 243
 aggttaagtcc cagtttgaag ctcaaaagat ctggtatgag cataggctca tcgacgacat 60
 ggtggccaa gctatgaaat cagaggagg cttcatctgg gcctgtaaaa actatgtatgg 120
 tgacgtgcag tggactctg tggcccaagg gtatggctct ctcggcatga tgaccagcgt 180
 gctggttgt ccagatggca agacagtaga agcagaggct gcccacggga ctgtAACCG 240
 tcactaccgc atgttccaga aaggacagga gacgtccacc aatcccattt cttccatttt 300
 t 301

<210> 244
 <211> 300
 <212> DNA
 <213> Homo sapien

<400> 244
 gctggtttgc aagaatgaaa tgaatgattc tacagctagg acttaacctt gaaatggaaa 60
 gtcatgcaat cccatttgca ggatctgtct gtgcacatgc ctctgttagag agcagcattc 120

ccagggacct tggaaacagt tgacactgta aggtgcttgc tcccccaagac acatcctaaa	180
aggtgttcta atggtgaaaaa cgtcttcctt ctttattgcc ccttcttatt tatgtgaaca	240
actgtttgtc ttttgttat ctttttaaa ctgtaaaggta caattgtgaa aatgaatac	300
<210> 245	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 245	
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tatatactta gataaaaaat gaggtgaaatt actatccatt gaaatcatgc tcttagaatt	120
aaggccagga gatattgtca ttaatgtara cttcaggaca ctagagtata gcagccctat	180
gttttcaaag agcagagatg caattaaata ttgttttagca taaaaaggc cactcaatac	240
agctaataaa atgaaagacc taatttctaa agcaattctt tataatttac aaagttttaa	300
g	301
<210> 246	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 246	
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acctgggctt atttaaaga actattgtt gctcagattt gttttcttat ggctaaaata	120
agtgccttctt gtggaaaatta aataaaacag ttaattcaaa gccttgatata atgttaccac	180
taacaatcat actaaatata ttttgaagta caaagtttga catgcctaa agtgacaacc	240
caaatgtgtc ttacaaaaca cgttcctaacc aaggtagtgc ttacactacc aatgcagaaa	300
c	301
<210> 247	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 247	
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gcctaagagg gcgactggcg gcagcacaac caaggaaggc aagggttggg cccccacgct	120
gtgtcctgtg ttcaagggtcg acacacaatc ctcatggaa caggatcacc catgcgtgc	180
ccttgatgtat caagggtggg gcttaagtgg attaaggggag gcaagttctg ggttccttgc	240
cttttcaaaccatgaagtca ggctctgtat ccctcctttt cctaactgtat attctaacta	300
a	301
<210> 248	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 248	
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attaggaaga ttcttagggg taattttctt gaggaaggag aactagccaa ctttggaaatt	120
acaggaagaa agtggtttgg aagacagccaa aagaaataaa agcagattaa attgtatcag	180
gtacattcca gcgttggc aactccataaa aaacatttca gattttatc ccgaatttttag	240
ctaatgagac tggatttttg ttttttatgt tttgtgtcgc agagctaaaa actcagttcc	300
c	301
<210> 249	
<211> 301	

<212> DNA
 <213> Homo sapien

<400> 249
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 ccctgacgct gctgttctcc ccgaaaaacc cgaccgaccc cccgcatctc cgtcccggcc 120
 ccagggagac acagcagtga ctcagagctg gtcgcacact gtgcctccct cctcaccgccc 180
 catcgtaatg aattattttgg aaaattaatt ccaccatcct ttcagattct ggatggaaag 240
 actgaatctt tgactcagaa ttgtttctg aaaagaatga tgtgacttcc ttagtcattt 300
 a 301

<210> 250
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 250
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 cttatctta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc 120
 cataagcaca tcagttttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac 180
 ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgtat ttaaagacta 240
 caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc 300
 a 301

<210> 251
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 251
 gccgagggtcc tacatttggc ccagttccc cctgcacccct ctccagggcc cctgcctcat 60
 agacaacctc atagagcata ggagaactgg ttgccttggg ggcaggggga ctgtctggat 120
 ggcaggggtc ctcaaaaatg ccactgtcac tgccagggaaa tgcttctgag cagtagaccc 180
 cattgggatc aatgaaaagc ttcaagaaat cttcaggctc actctcttgc aggccccggaa 240
 cctctggagg gggcagtgaaatccagct ccaggacggaa tcctgtcgaa aagatatcc 300
 c 301

<210> 252
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 252
 gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgtgg catttcctca 60
 ttttctacat tggaaatca agagttaaa taaatgtata tcgatgtctt caagaatata 120
 tcatttcctt ttcaacttagga acccatcaa aatataagtc aagaatctt atatcaacaa 180
 atatatacaag caaactggaa ggcagaataa ctaccataat ttgtataag tacccaaagt 240
 tttataaattc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc 300
 a 301

<210> 253
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 253
 ttccctaaga agatgttatt ttgttgggtt ttgttcccccc tccatctcga ttctcgtaacc 60
 caactaaaaaa aaaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctcccttagct 120

tggtcgtatt gtttcagac cttaaaatat aaacttgtt cacaagctt aatccatgtg	180
gatttttttt cttagagaac cacaaaacat aaaaggagca agtccggactg aataccttt	240
tccatagtgc ccacaggta ttccctcacat ttctccata ggaaaatgct tttcccag	300
g	301
<210> 254	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 254	
cgctgcgcct ttcccttggg ggaggggcaa ggccagaggg ggtccaagtg cagcacgagg	60
aacctgacca attcccttga agcgggtggg taaaccctg taaatggaa caaaatcccc	120
ccaaatctct tcatacttacc ctggggact cctgactgta gaatttttg gttgaaaacaa	180
aaaaaaaata aagctttgga ctttcaagg ttgcttaaca ggtactgaaa gactggcctc	240
acttaaactg agccagggaa agctgcagat ttataatgg gtgtgttagt gtgcagtgcc	300
t	301
<210> 255	
<211> 302	
<212> DNA	
<213> Homo sapien	
<400> 255	
agcttttttt tttttttttt ttcattaaaa aatagtgttc tttattataa	60
attactgaaa tgtttctttt ctgaatataa atataaataat gtgcaaagtt tgacttggat	120
tgggatttttgg tttagttctt caagcatctc ctaataccctt caaggccctg agtaggggggg	180
aggaaaaaagg actggggatgtt gaatctttat aaaaaacaag agtgatttgag gcagattgtt	240
aacattatta aaaaacaaga aacaaacaaa aaaatagaga aaaaaccac cccaaacacac	300
aa	302
<210> 256	
<211> 301	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(301)	
<223> n = A,T,C or G	
<400> 256	
gttccagaaa acattgaagg tggcttccca aagtctaact agggataccc cctctagcct	60
aggaccctcc tccccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc	120
accccaaaaa gcctggacac cttgagcaca cagttatgac caggacagac tcatacttat	180
aggcaaatacg ctgctggcaa actggcatta cttggttgtt gggatgggg gggcaagtgt	240
gtggcccttc ggcctggta gcaagaacat tcaggtagg cctaagttt tcgtgttagt	300
t	301
<210> 257	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 257	
gttgtggagg aactctggct tgctcattaa gtcctactga ttttcaactat cccctgaatt	60
tccccactta tttttgtctt tcactatcgc aggccctaga agaggtctac ctgcctccag	120
tcttacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat	180

gtcacattac tcccttcagt gatttttgtt agaagtgccta atccctgaat gccaccaaga	240
tcttaatctt cacatctta atcttatctc tttgactcct ctttacaccg gagaaggctc	300
c	301

<210> 258
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 258

cagcagtagt agatgccgtt tgccagcactc cccagcactc ccaggatcg caccagcacc	60
agggggcccg ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc	120
cccaggccaa caagaatcca ataccaggac tgggcaaaaat cttcaaaat cttaaactg	180
atgtctcggtt cattgaggct gtcaataana cgctgatccc ctgctgtatg gtgggtcat	240
tggtgatccc tgggagcgcc ggtggagtaa cggtggatcca tggaaagcag cgccccacaac	300
t	301

<210> 259
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 259

tcatatatgc aaacaaaatgc agactangcc tcagggcagag actaaaggac atctttggg	60
gtgtcctgaa gtgatttggc cccctgaggg cagacaccta agtaggaatc ccagtggaa	120
gcaaaggccat aaggaagccc aggattctt gtgatcagga agtgggcccag gaaggtctgt	180
tccagctcac atctcatctg catgcagcac ggaccggatg cgcccaactgg gtcttggctt	240
ccctcccatc ttctcaagca gtgtccttgt tgagccattt gcatccttgg ctccaggtgg	300
c	301

<210> 260
<211> 301
<212> DNA
<213> Homo sapien

<400> 260

ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaaata aagcaatgg	60
aagggtctt aacttgaaaa agattaggag tcactggttt acaagttata attgaatgaa	120
agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaaca caggattaac	180
tagggcaaaa taaaataagtg tgtggaaagcc ctgataagtg cttataaaac agactgattc	240
actgagacat cagtacctgc ccggccggcc gctcgagccg aattctgcag atatccatca	300
c	301

<210> 261
<211> 301
<212> DNA
<213> Homo sapien

<400> 261
 aaatattcga gcaaattctg taactaatgt gtctccataa aaggcttga actcagtcaa 60
 tctgcctcca tccacgattc tagcaatgac ctctcgaca tcaaagctcc tcttaaggtt 120
 agcaccaact attccataca attcatcagc aggaataaaa ggctcttcag aaggttcaat 180
 ggtgacatcc aatttcttct gataatttag attcctcaca accttcctag ttaagtgaag 240
 ggcatgatga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc 300
 a 301

<210> 262
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 262
 gaggagagcc tgttacagca tttgttaagca cagaatactc caggagtatt tgtaattgtc 60
 tgtgagcttc ttgccgcaag tctctcagaa attttaaaag atgcaaatcc ctgagtcacc 120
 cctagacttc ctaaacccaga tcctctgggg ctggaacctg gcactctgca tttgttaatga 180
 gggcttctg gtgcacaccc aattttgtgc atcttgc(cc) taaatcctgg attagtgc(cc) 240
 catcattacc cccacattat aatggatag attcagagca gatacttcc agcaaagaat 300
 c 301

<210> 263
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 263
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 aaaattacta ctaatccta attcacaata acaatggcat taaggttga cttgagttgg 120
 ttcttagtat tattttatggt aaataggctc ttaccacttg caaataactg gccacatcat 180
 taatgactga ctccccagta aggctctcta agggtaagt angaggatcc acaggatttg 240
 agatgctaag gccccagaga tcgtttgatc caacccttattttcagag gggaaaatgg 300
 g 301

<210> 264
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 264
 aaagacgtta aaccactcta ctaccacttg tggaaactctc aaaggtaaaa tgacaaaasc 60
 aatgaatgac tctaaaaaca atatttacat ttaatggtt gtagacaata aaaaaacaag 120
 gtggatagat ctagaattgt aacattttaa gaaaaccata scatttgaca gatgagaaaag 180
 ctcattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240
 acccttcata taaatttact atcttggtt gaggcactcc ataaaatgtt tcacgtgcat 300
 a 301

<210> 265
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 265

tgcccaagtt atgtgttaat gatatccac ccagaggtaa aactacactg tcatacttgc	60
cttcttgtga cgcaatgtattt ctatctggg gagaagcccg gaagtcttct cttggctcta	120
catattcttgc gaagtctcta atcaactttt gtccatattt tttcattttt tcaggaggaa	180
ttttcagttt gtcaacatgt tctctaaca cacttgccca tttctgtaaa gaatccaaag	240
cagtccaaagg ctttgacatg tcaacaacca gcataactag agtataccttc agagatacgg	300
c	301
<210> 266	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 266	
taccgtctgc ctttctccc atccaggcca tctgcaatc tacatgggtc ctcctattcg	60
acaccagatc actctttctt ctacccacag gtttgcatacg agcaagagac acaacccct	120
ctttctgtt ttccagttt tttctgtt ctcccaccc ctttgcatacg attcctgggg	180
atagagacac caataccat aacctcttc ctaaggctcc ttataacccaa-ggggtgcacag	240
cacagactcc tgacaactgg taaggccat gaactggtag ctcacagctg gctgtgcctg	300
a	301
<210> 267	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 267	
aaagagacaca ggccagctca gcctgcctg gcatctaga ctcagcctgg ctccatgggg	60
gttctcagtgt ctgagttccat ccaggaaaag ctcacctaga ctttctgtt ctgaatcttc	120
atcccteacag gcagcttctg agagcctgtt atccctagcc ttatgtggct ggagtaaagc	180
ctcattctgtt ttccctcttctt tttttctttt caagttggct ttccctcacat ccctctgttc	240
aattcgttcc agcttgcgtt ctttagccctt catttccaga agcttcttctt ctttggcattc	300
t	301
<210> 268	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 268	
aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctggagt ttctttctta	60
gatcttggga gagctgggtt ttcttaaggag aaggaggaag gacagatgtt actttggatc	120
tcgaagagga agtctaattttt aagtaattttt tcaacgggtcc ttgttttagac tcttggaaata	180
tgctgggtgg ctcaatgttcc cttttttggag aaagcaagttt ttatttttttggatc ggagtaacca	240
cttcccatttgc ttctactttt taccatcatc aattgttat tatgtattttt ttggagaact	300
a	301
<210> 269	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 269	
taacaatata cacttagctat ctttttaact gtccatcatt agcaccaatg aagattcaat	60
aaaattttttt acctttttttt ttattttttt atctcaaaac aattttttttt attttttttt aagttttttt	120
atagtccacat acctttttttt ttccatattttt tttttttttt tactttttttt aagttttttt	180
ctttttttttt tttttttttt aaaatttttt taaaattttttt ggtttttttt ccccccaattttttttt	240
tacagttagca caaccacccat atgtttttttt tacatgtatag ctctgttagaa gttttttttt	300
t	301

<210> 270
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 270
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 cacaagaata catattcctt ttatttctaa ggaggtaaac atagatgttag ctgatgtgga 120
 gagcttgctg gtgcagtgca tattggataa cactattcat ggccgaatttgc atcaagtcaa 180
 ccaactcctt gaactggatc atcagaagaa ggggtggtgca cgatatactg cactagataa 240
 tggaccaacc aactaaatttctc tctcaccagg ctgtatcagt aaactggctt aacagaaaac 300
 a 301

<210> 271
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 271
 aaaagttct cataagatta acaattttaa taaatatttgc atagaacatt ctttctcatt 60
 tttatagctc atcttttaggg ttgatattca gttcatgctt cccttgcgt tcttgatcca 120
 gaartgcaat cacttcatca gcctgtatttgc gctccaatttgc tctataaagt gggtccaagg 180
 tgaaccacag agccacagca caccttttc ccttggtgac tgccttcacc ccatganggt 240
 tctctccccc agatganaac tgatcatgca cccacattttt gggtttata gaagcagtca 300
 c 301

<210> 272
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 272
 taaattgcta agccacagat aacaccaatc aaatggaaaca aatcaactgtc ttcaaatgtc 60
 ttatcagaaa accaaatgag ccttggatct tcataatacc taaacatgcc gtattttagga 120
 tccaaataatt ccctcatgtatc gagcaagaaa aattctttgc gcacccctcc tgcattccaca 180
 gcatcttctc caacaaatat aaccttggatc ggcttcttgc aatctatgtt ctttgggg 240
 ctaaggactt ccattgcattc tcctacaata ttttctctac gcaccactag aattaaggcag 300
 g 301

<210> 273
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 273
 acatgtgtgt atgtgtatct ttggggaaaan aanaagacat cttgttayt attttttgg 60
 agagangctg ggacatggat aatcacwtaa ttgtctayta tyactttaat ctgactyga 120

gaaccgtcta aaaataaaat ttaccatgtc dtatattcct tatagtatgc ttatccacc	180
ttyttctgt ccagagagag ttcgtgtac ananatttma gggtaamac atgmattgg	240
gggacttny ttacngagm accctgccc sgccctcg makcngantt ccgcsananc	300
t	301
<210> 274	
<211> 301	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(301)	
<223> n = A,T,C or G	
<400> 274	
cttatatact cttctcaga ggcaaaagag gagatggta atgtagacaa ttcttgagg	60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaaatt aacttgtaaa	120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttgc gaaaaagtcca	180
tctaggatg gttgcattct cgtcttctt tctgcagtag ataatgaggt aaccgaaggc	240
aatttgtctt ctttgataa gaagcttct tggcatatc aggaaattcc aganaaaagtc	300
c	301
<210> 275	
<211> 301	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(301)	
<223> n = A,T,C or G	
<400> 275	
tcgggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agccaaacc acagaaaatg	60
gggtgaaatt ggccaacttt ctattaactt atgttggcaa tttgccacc aacagtaagc	120
tggccctct aataaaaagaa aattgaaagg ttctcaacta aacggaatta agtagtggag	180
tcaagagact cccaggcctc agcgtacctg cccggcggc cgctgaagc cgaattctgc	240
agatatccat cacactggcg gnccgtcgan catgcatactga aagggnccaa ttccgccttat	300
a	301
<210> 276	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 276	
tgtacacata ctcataataat aaatgactgc attgtggat tattactata ctgattatat	60
ttatcatgtg acttctaatt agaaaatgtt tccaaaagca aaacagcaga tataaaaaat	120
taaagagaca gaagatagac attaacagat aaggcaactt atacatgg aatccaaatc	180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttggt	240
aaaactatcc agtatgtttc cttgtttca tgtctgagaa ggctctcctt caatggggat	300
g	301
<210> 277	
<211> 301	
<212> DNA	
<213> Homo sapien	

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<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 277
tttgtatcg tcaatgtttt attacattgcg ttatgagtgc tcacctggaa aattctaaag      60
atacagagga ctggaggaa gcagagcaac tgaatttaat taaaagaag gaaaacattg      120
gaatcatggc actcctgata ctttccaaa tcaacactct caatgccca ccctcgtcct      180
caccatagtg gggagactaa agtggccacg gatttgcctt angtgtcag tgcgttctga      240
gttcnctgtc gattacatct gaccagtctc cttttccga agtcntccg ttcaatcttg      300
c                                         301

<210> 278
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 278
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aacatataa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgc      120
cagtctctac tggattatgt cattacctgg gaatttataat aagcccttaa taataatgc      180
aatgaacate tcatgtgtgc tcacaatgtt ctggcactat tataagtgtc tcacaggtt      240
tatgtttct tcgtaactt atggantagg tactcggccg cgaacacgct aagccgaatt      300
c                                         301

<210> 279
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 279
aaagcaggaa tgacaaagct tgctttctg gtatgttcta ggtgtattgt gactttact      60
gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc      120
ttagacctt accttccagc cacccacag tgcttgatat ttcagagtca gtcattgggt      180
atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac      240
catctgttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag      300
a                                         301

<210> 280
<211> 301
<212> DNA
<213> Homo sapien

<400> 280
ggtaactggag tttcctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg      60
tagaaaggtg gtgaaaccaa attgtgtca atggaaatag gagaatatgg ttctcactct      120

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tgagaaaaaaaa acctaaggatt agcccaggta gttgcctgta acttcagttt ttctgcctgg	180
gtttgatata gtttagggtt ggggttagat taagatctaa attacatcag gacaaagaga	240
cagactattta actccacagt taattaagga ggtatgttcc atgtttattt gttaaaggcag	300
t	301
<210> 281	
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<212> DNA	
<213> Homo sapien	
<400> 281	
aggtaacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatattc	60
gccgagcaat ccaaatacctg aatgaagggg catcttctga aaaaggagat ctgaatctca	120
atgtggtagc aatggcttta tcgggttata cgatgagaa gaactccctt tggagagaaa	180
tgtgttagcac actgcgatta cagctaaata acccgatttt gtgtgtcatg ttgcatttc	240
tgacaagtga aacaggatct tacgatggag tttgtatga aaacaaagtt gcagtacctc	300
g	301
<210> 282	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 282	
caggtactac agaattaaaa tactgacaag caagtagttt cttggcgtgc acgaattgca	60
tccagaaccc aaaaattaag aaattcaaaa agacattttg tgggcacctg ctagcacaga	120
agcgcagaag caaagcccag gcagaaccat gctaaccctt cagctcagcc tgcacagaag	180
cgcagaagca aagcccaggc agaaccatgc taaccttaca gtcagcctg cacagaagcg	240
cagaagcaaa gcccaggcag aacatgctaa cttacagct cagctgcac agaagcacag	300
a	301
<210> 283	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 283	
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cactttgagg gcttataat aatatgtgc ttgaaaaaaaaaa aaatgtgttag ttgatactca	120
gtgcacatcc agacatagta aggggttgct ctgaccaatc aggtgatcat ttttctatc	180
acttcccagg ttttatgcaa aaattttgtt aaattctata atggtgatat gcatctttt	240
gaaaaacatat acattttaa aaatctattt tatgtaaagaa ctgacagacg aatttgctt	300
g	301
<210> 284	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 284	
caggtacaaa acgttattaa gtggctttaga atttgaacat ttgtgtctt tattttacttt	60
gcttcgtgtg tggccaaagc aacatcttcc ctaaatatat attaccaaga aaagcaagaa	120
gcagattagg ttttgacaa aacaaacagg cccaaagggg gctgacctgg agcagagcat	180
ggtgagaggc aaggcatgag agggcaagtt ttttgtggac agatctgtgc ctactttatt	240
actggatcaa aagaaaaacaa agttcattga tttgtcaagga tatatacagt gtttagaaatt	300
a	301
<210> 285	

<211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 285

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aatgatcatt agtgtttaa aaaaaatact gaaaactcct tctgcattccc aatctctaac	120
caggaaagca aatgttattt acagacctgc aagccctccc tcaaachaaa ctatttctgg	180
attaaatatg tctgacttct tttaggtca cacgactagg caaatgctat ttacgatctg	240
caaaagctgt ttgaagagtc aaagccccca tgtgaacacg atttctggac cctgttaacag	300
t	301

<210> 286
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 286

taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct	60
tgttatattt ttttgcccta cagtggatca ttcttagtgg aaaggacagt aagattttt	120
atcaaaatgt gtcatgccag taagagatgt tatattttt tctcatttct tccccaccca	180
aaaataagct accatatagc ttataagtct caaatttttgc cttttacta aatgtgatt	240
gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt tttcccttg	300
t	301

<210> 287
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 287

tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg	60
cccagaagga acgttagagat cagatattac aacagctttg ttttgagggt tagaaatatg	120
aatatgtttt gttatgaacg cacagtttag gcagcaggcc cagaatcctg accctctgcc	180
ccgtggttat ctcccccac gcttggctgc ctcatgttat cacagtattc cattttgttt	240
gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttccctca ttggtaatgc	300
t	301

<210> 288
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 288

gtacacctaa ctgcaaggac agctgaggaa tggtaatgggc agccgctttt aaagaagtag	60
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgaa agctgaaaaa	120
gatctttaaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatac	180
aaaagcatct gctttgtga tttaatttag ctcatctggc cactggaga atccaaacag	240
tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaaaa	300
a	301

<210> 289
 <211> 301

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<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 289
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gcttttgatg tctccaagta gtccacccctc atttaactct ttgaaactgt atcatctttg     120
ccaagtaaga gtgggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa     180
cggtctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaaga     240
tgtgtttgt tttggactct ctgtggtccc ttccaatgct gtgggttcc aaccagngga     300
a                                         301

<210> 290
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 290
acactgagct ctctttgata aatatacaga atgcttggca tatacaagat tctatactac      60
tgactgatct gtcattttct ctcacagctc ttacccccaa aagctttcc accctaagtg     120
ttctgacctc cttttctaat cacagtaggg atagaggcag anccacctac aatgaacatg     180
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg cttagcagtgc     240
tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagttag     300
a                                         301

<210> 291
<211> 301
<212> DNA
<213> Homo sapien

<400> 291
caggtaccaa tttcttctat cctagaaaaca tttcattttt tgttgttcaa acataacaac      60
tatatcagct agatttttt tctatgcttt acctgctatg gaaaatttga cacattctgc     120
tttactctt tgtttatagg tgaatcacaa aatgttattt tatgtattct gtatgttcaat     180
agccatggct gtttacttca tttttttat tttagcataaa gacattatga aaaggcctaa     240
acatgagctt cacttccccca ctaactaatt agcatctgtt atttcttaac cgtaatgcct     300
a                                         301

<210> 292
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 292

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 aaaaccaag natataaccg aaaggaaaaa cagatgagac ataaaatgtat ttgcnagatg 180
 gaaaaatatacg tasttyatga atgttnatta aattccaggat ataatagtgg ctacacactc 240
 tcactacaca cacagacccc acagtcctat atgccacaaa cacattcca taacttgaaa 300
 a 301

<210> 293
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 293

ggtaccaagt gctgggtgcca gcctgttacc tgttctcaact gaaaagtctg gctaattgctc 60
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 aacacaaaacg tcactagcaa agtagcaaca gcttaagtc taaatacaaa gctgttctgt 180
 gtgagaattt tttaaaaggc tacttgtata ataacccttg tcattttaa tgtacctcg 240
 ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gctcgagcat 300
 g 301

<210> 294
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 294

tgaccctataa caatatacac tagcttatctt tttaactgtc catcattagc accaatgaag 60
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 tttaactata gtcacaganc ttaaatattt acattgtttt ctatgtctac tgaaaataag 180
 ttcaactactt ttctgggata ttcttacaa aatcttatta aaattcctgg tattatcacc 240
 cccaaattata cagtagcaca accacctt gtatttta catgatagct ctgttagaggt 300
 t 301

<210> 295
 <211> 305
 <212> DNA
 <213> Homo sapien

<400> 295

gtactcttc tctccccctcc tctgaatttta attctttcaa cttgcaattt gcaaggattt 60
 cacatttcac tttgtatgtat attgtgttgc aaaaaaaaaaa gtgtcttgc ttaaaattac 120
 ttggtttgc aatccatctt gcttttccc catttggact agtcatcaac ccatctctga 180
 actggtagaa aaacrtctga agagcttagtc tatcagcattt tgacaggtga attggatgg 240
 tctcagaacc attcacccca gacagcctgt ttctatcctg tttaataat tagttgggt 300
 tctct 305

<210> 296
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 296

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caccttagtag taaaactaaaa ataaaactgaa acttttatgga atctgaagtt attttccttg	120
ataaaataga attaataaaac caaatatgagg aaacatgaaa ccatgcaatc tactatcaac	180
tttggaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtatt	240
tgtcattact ataaaatttttta aaatctgtta ataagatggc ctatagggag gaaaaagggg	300
c	301
<210> 297	
<211> 300	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(300)	
<223> n = A,T,C or G	
<400> 297	
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aagggtttga aaaccttgaa ggagaatcat ttgacaaga agtacttaag agtctagaga	120
acaaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttggtaggcctgt	180
tccatcatttggagtgact ggccatccct caaaaattttgt ctgggctggc ctgagtggtc	240
accgcacccgcacc acgctaagcc gaattctgca gatattccatc acactggcgg	300
<210> 298	
<211> 301	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(301)	
<223> n = A,T,C or G	
<400> 298	
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ggcatctgag agacctggtg ttccagtgtt tctggaaatg ggtcccagtgc cccggcgtcg	120
tgaagctctc agatcaatca cgggaaggcc ctggcggtgg tggccacctg gaaccaccct	180
gtcctgtctg tttacatttc actaycaggt ttctctggg cattacnatt tttccctta	240
caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcaggtggct ctcagcgagg	300
t	301
<210> 299	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 299	
gttttgagac ggagttcac tcttggcc cagactggac tgcaatggca gggctctgc	60
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tgggattgca ggctcaegcc accataacca gctaattttt ttgtatattt agtagagacg	180
gagtttcgcc atgttggcca gctggctca aactcctgac ctcaagcgac ctgcctgcct	240
cggcctccca aagtgctgga attataggca ttagtcaaca cgccccagcct aaagatattt	300
t	301
<210> 300	
<211> 301	
<212> DNA	
<213> Homo sapien	

<400> 300
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tatgtcccc acccaactggg aaaggctccc acctggctac ttcccttatac agctgggtca 120
gctgcattcc acaaggttct cagcctaatt agtttacta cctgccagtc tcaaaaactta 180
gtaaagcaag accatgacat tcccccacgg aaatcagagt ttgccccacc gtcttgta 240
tataaaagcct gcctctaaca gtcctgctt cttcacaccca atcccgagcg catccccat 300
g 301

<210> 301
<211> 301
<212> DNA
<213> Homo sapien

<400> 301
ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcaagtctgc 60
agaggacccc agtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagtttgt 120
gggaactcac aaagaccctc agagctgaga cacccacaac agtggagact cacaagacc 180
ctcagagctg agacacccac aacagtggg gtcacaaag accctcagag ctgagacacc 240
cacaacagca ctcgttcag ctgcccacatg tgtgaataag gatgcaatgt ccagaagtgt 300
t 301

<210> 302
<211> 301
<212> DNA
<213> Homo sapien

<400> 302
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tgaattttga aaatttactac ttaatctaa ttccacaataa caatgcatt aaggtttgac 120
ttgagtttgt tccttagtatt atttatggta aataggctct taccacttgc aaataactgg 180
ccacatcatt aatgactgac ttcccagtaa ggctctctaa gggtaagta ggaggatcca 240
caggatttga gatgctaagg ccccagagat cgtttgcattt aaccctctta ttttcagagg 300
g 301

<210> 303
<211> 301
<212> DNA
<213> Homo sapien

<400> 303
aggtaccaac tggaaata ggttagaggat catttttctt ttccatatca actaagttgt 60
atatttttt ttgacagttt aacacatctt cttctgtcag agatttttc acaatagcac 120
tggctaatgg aactaccgct tgcattaa aatgggttgt ttgtgaaatg atcataggcc 180
agtaacgggt attttttctt aactgatctt ttgctcgatc caaaggacc tcaagacttc 240
catcgatttt atatctgggg tctagaaaag gagttatct gttttccctc ataaattcac 300
c 301

<210> 304
<211> 301
<212> DNA
<213> Homo sapien

<400> 304
acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgcctaat 60
tatttagttt agtttcagct taccctactt ttgtctgcaa catgcaraas agacagtgc 120
cttttttagtg tatcatatca ggaatcatct cacattgggt tgcatttttgcactt 180
gactttcagc cacttggta aggtggagtt ggccatatgt ctccactgca aaattactga 240

ttttcccttt gtaattaata agtgtgttg tgaagattct ttgagatgag gtatatatct	300
c	301
<210> 305	
<211> 301	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(301)	
<223> n = A,T,C or G	
<400> 305	
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cagggggaca gacctggaca gacacgttgc catttgcgtgc tgtggtagg aaaatggcg	120
taaaggagga gaaacagata caaaatctcc aactcgtat taaggatttc tcattgcctag	180
aatattggta gaaacaagaa tacattcata tgcaaataa ctaaccatgg tggaaacaaa	240
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag	300
a	301
<210> 306	
<211> 8	
<212> PRT	
<213> Homo sapien	
<400> 306	
Val Leu Gly Trp Val Ala Glu Leu	
1	5
<210> 307	
<211> 637	
<212> DNA	
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<400> 307	
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attgaggaat gatacttgag cccaaagagc attcaatcat tttttttt gcctttttt	180
cacaccattt gtgagggagg gattaccacc ctggggttat gaagatggtt gaacacccca	240
cacatagcac cggagatatg agatcaacag ttcttagcc atagagattc acagcccaga	300
gcaggaggac gctgcacac catcaggat gacatggggg atgcgtctgg gattgggttg	360
aagaagcaag gactgttaga ggcaggctt atagaacaa gacgggggg caaactctga	420
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtgtgaa	480
actcattagg ctgagaacct tggaaatgc acttgaccca sctgatagag gaagtagcca	540
ggtgggagcc tttcccagtg ggtgtggac atatctggca agatttgtg gcaactcctgg	600
ttacagatac tggggcagca aataaaactg aatcttg	637
<210> 308	
<211> 647	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(647)	
<223> n = A,T,C or G	

<400> 308

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tgctcagggg aaggttcata	tgggacttgc tactgccccaa gtttctatac aggtataaa	120
ggngcctcac agtata	gtc actgaaa gaagaagaaa caaacactga tctcttctg	180
ccaccctct gacccttgg	aactcctctg accctttaga acaaggctac ctaatatctg	240
ctagagaaaa gaccaacaac	ggcctcaaag gatctttac catgaaggtc tcagctaatt	300
cttggtaag atgtgggtc	cacattaggt tctgaatatg gggggaaaggg tcaatttgct	360
catttgtgt gtggataaaag	tcaggatgcc caggggcccag agcagggggc tgcttgctt	420
gggaacaatg gctgagcata	taaccatagg ttatggggaa caaaacaaca tcaaagtac	480
tgtatcaatt gccatgaaga	cttgaggac ctgaatctac cgattcatct taaggcagca	540
ggaccagttt gagtggcaac	aatgcagcag cagaatcaat ggaaacaaca gaatgattgc	600
aatgtccccc ttttctcct	gcttcgtact tgataaaaagg ggaccgt	647

<210> 309

<211> 460

<212> DNA

<213> Homo sapien

<400> 309

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aatatgattt gctgcacact	tccagactga tgaatgtga acgtgatgga ctattgtatg	120
gagcacatct tcagcaagag	ggggaaatac tcatcatttt tggccagcag ttgtttgatc	180
accaaacatc atgcca	gaaat actcagcaaa ctttcttage ttttggaaag tcaaagtccg	240
ggggaaattt ttcctggcaa	tttttaattgg actcctttagt tgagagcagc ggctacccag	300
ctgggggtgtt ggagcgaacc	cgtcaactgtt ggacatgcag tggcagagct cctggtaacc	360
acctagagga atacacagggc	acatgtgtga tgccaagegt gacacctgta gcactcaa	420
ttgttcttgc tttgtcttc	ggtgtgtaaat ttcttaagt	460

<210> 310

<211> 539

<212> DNA

<213> Homo sapien

<400> 310

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ctaaaggttt taaaatatgt	caggattgga agaaggcatg gataaagaac aaagttcagt	120
taggaagag aaacacagaa	ggaagagaca caataaaaagt cattatgtat tctgtgagaa	180
gtcagacagt aagatttgc	ggaaatgggt tggtttgc tatggatgt atttttagcaa	240
taatctttat ggcagagaaa	gctaaaatcc tttagcttgc gtgaatgatc acttgcgtaa	300
ttcctcaagg taggcataat	gaaggagggt ttagaggaga cacagacaca atgaactgac	360
ctagatagaa agccttagta	tactcagcta ggaatagtga ttctgaggc acactgtgac	420
atgattatgt cattacatgt	atggtagtga tggggatgtat aggaaggaag aacttatggc	480
atattttcac cccccacaaaaa	gtcagttaaa tattggaca ctaaccatcc aggtcaaga	539

<210> 311

<211> 526

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(526)

<223> n = A,T,C or G

<400> 311

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ttttgacgtt ttctctaaac	tactaaagag gcattaatga tccataaatt atattatcta	120
catttacagc attaaaaatg	tgttcagcat gaaatattag ctacagggga agctaaataa	180

attaaacatg gaataaaagat ttgtccttaa atataatcta caagaagact ttgatatttgc	240
ttttcacaa gtgaagcatt cttataaaagt gtcataacct ttttgggaa actatggaa	300
aaaatgggaa aactctgaag ggtttaagt atcttacctg aagctacaga ctccataacc	360
tctcttaca gggagctcct gcagccctca cagaaatgag tggctgagat tcttgattgc	420
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agtctataa actgttagtnt acttattttc atccccaaag cacagt	526
<210> 312	
<211> 500	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(500)	
<223> n = A,T,C or G	
<400> 312	
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tcatttctga aagcaggta gccactttat tccaaagtac actgcagatg ttcaaactct	120
ccatttctct ttcccttcca cctgcaagtt ttgctgactc tcaacttgc atgagtgtaa	180
gcattaagga cattatgctt ctgcattctt gaagacaggc cctgctcatg gatgactctg	240
gcttcttagg aaaatatttt tcttccaaaa tcagtaggaa atctaaactt atccccctctt	300
tgcagatgtc tagcagcttc agacattgg ttaagaaccc atggaaaaaaa aaaaaatccot	360
tgctaatgtg gtttccttgc taaaccanga ttcttatttg nctggtatag aatatcagct	420
ctgaacgtgt ggtaaagatt tttgtgtttt aatataggag aaatcagttt gctgaaaagt	480
tagtettaat tatctattgg	500
<210> 313	
<211> 718	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(718)	
<223> n = A,T,C or G	
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ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa	180
gtatgtacat gttttgcac atttccagcc cttttaataa tccacacaca caggaagcac	240
aaaaggaagc acagagatcc ctggggaaaaa tgcccgcccg ccatcttggg tcatcgatga	300
gcctcgccct gtgcctgntc ccgcttgtga gggaggaca tttagaaaatg aattgtatgt	360
ttccttaaag gatggcagga aaacagatcc tgggtgttatttga acgggattac	420
agatttgaaa tgaagtcaca aagtggcat taccatgag aggaaaacag acgagaaaat	480
cttgcattgtt cacaagacat gcaacaaaca aaatggataa ctgtgcattgc acggcagcc	540
aactggggag gagataccac gggggcagagg tcaggattctt ggcctgtctg cctaactgtg	600
cgttatacca atcatttcta tttctaccct caaacaagct gtngaatatc tgacttacgg	660
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<210> 314	
<211> 358	
<212> DNA	
<213> Homo sapien	
<400> 314	

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caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg tgttagtccaa	180
gctctcgta gtcacggcac tgtaaacat gtcaccccta gattaacctc gtggacgctc	240
ttgttgtatt gctgaactgt agtgcctgt attttgcctc tgtctgtgaa ttctgttgc	300
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<210> 315	
<211> 341	
<212> DNA	
<213> Homo sapien	
<400> 315	
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gaccggcatt ctgaagatgt ctggAACCTC taccagcagg atgatgatag ccccaatgac	180
agtcaccagc tccccgacca gcccggatatc gtccttaggg gtcatgtagg cttctgtaa	240
tagttctgc tgcgtggccg tgtaagaggg tggtgtcccg ggggctcggt cggttattgg ttctgggctt	300
gaggggggcg tagatgcagc acatggtaaa gcaatgtatg t	341
<210> 316	
<211> 151	
<212> DNA	
<213> Homo sapien	
<400> 316	
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cattcaggga gtcgtgggtt caatattttt a	151
<210> 317	
<211> 151	
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<213> Homo sapien	
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<213> Homo sapien	
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tggggccgtt ttagtcaaggca gtgataaaaca t	151
<210> 319	
<211> 151	
<212> DNA	
<213> Homo sapien	
<400> 319	
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catagatagt actaggtatt aatagatatg taaagaaaga aatcacacca ttaataatgg	120

taagattggg tttatgtat tttatgtgggt a	151
<210> 320	
<211> 150	
<212> DNA	
<213> Homo sapien	
 <400> 320	
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gaggcgctgc cctttttttt ttttttttgggggaaatt tttttttttaatagttatt	120
gagtgttcta cagttacag taaataccat	150
<210> 321	
<211> 151	
<212> DNA	
<213> Homo sapien	
 <400> 321	
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tagggggca ttgttaaccag ctatggcata ggtgttaacc aaaggcttag taaacatggg	120
tgcctctgag aaatcaaagt cttcatacac t	151
<210> 322	
<211> 151	
<212> DNA	
<213> Homo sapien	
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<223> n = A,T,C or G	
 <400> 322	
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attgtgcagg gctcgcttca nacttccagt t	151
<210> 323	
<211> 151	
<212> DNA	
<213> Homo sapien	
 <220>	
<221> misc_feature	
<222> (1)...(151)	
<223> n = A,T,C or G	
 <400> 323	
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nagactcant tactacccag tttgtgttt twtgggagaa atgtaactgg acagtttagct	120
gttcaatyaa aaagacactt ancccatgtg g	151
<210> 324	
<211> 461	
<212> DNA	
<213> Homo sapien	
 <220>	

<221> misc_feature
 <222> (1)...(461)
 <223> n = A,T,C or G

<400> 324

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agagttacta cgaatcccat ctgggtcca gctatatcac tgacagcatg gttagaagact	180
gcgaacctca cttctagact ttcacggtgg gacgaaacgg gttcagaaac tgccaggggc	240
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cacacaaaatg caatagttgg tcactgcatt ttacctgaa ccaaagctaa accccgggttt	360
gccaccatgc accatggcat gccaggttc aacactgtt ctcttggaaaa ttgggtctga	420
aaaaacgcac aagagccctt gcctgcctt agctgangca c	461

<210> 325

<211> 400
 <212> DNA
 <213> Homo sapien

<400> 325

acactgtttc catgttatgt ttctacacat tgctaccta gtgctctgg aaacttagct	60
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agtaagagtg gtggcttatt tcagctgtt tgacaaaaatg actggctct gacttaacgt	180
tctataaaatg aatgtgttga agcaaagtgc ccatggtggc ggcgaagaag agaaagatgt	240
gttttggggggactctctg ttgtcccttc caatgtgtt ggtttccaaac caggggaagg	300
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<210> 326

<211> 1215
 <212> DNA
 <213> Homo sapien

<400> 326

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ttaactctgg ggactggaa cccatgaaat tgaccccccatacatcccg cggagggaaat	720
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acagtgcggcc cttgtggcac gttgacccaa ctttaccatgt tggttttca tttttgtcc	1140
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aaaaaaaaaaaaaaa aaaaa	1215

<210> 327

<211> 220

<212> PRT
<213> *Homo sapien*

<400> 327
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 Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
 20 25 30
 Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
 35 40 45
 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
 50 55 60
 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
 65 70 75 80
 Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
 85 90 95
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
 100 105 110
 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
 115 120 125
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
 130 135 140
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
 145 150 155 160
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
 165 170 175
 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
 180 185 190
 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
 195 200 205
 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 210 215 220

<210> 328
<211> 234
<212> DNA
<213> *Homo sapien*

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<400> 328
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atcccgagtg ggtgctgtca gccacacact gttccagaa ctcctacacc atcgggctgg 180
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<210> 329
<211> 77
<212> PRT
<213> *Homo sapien*

<400>	329														
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					20					25				30	
Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln	Trp	Val	Leu	Ser	Ala	Thr
					35				40				45		
His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly	Leu	Gly	Leu	His	Ser	Leu
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Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala
65 70 75

<210> 330
<211> 70
<212> DNA
<213> Homo sapien

<400> 330
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qctqcaqcca 70

<210> 331
<211> 22
<212> PRT
<213> *Homo sapien*

<400> 331
 Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu
 1 5 10 15
 Val Ser Gly Ser Cys Ser
 20

<210> 332
<211> 2507
<212> DNA
<213> *Homo sapien*

<400>	332					
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cccaggaact	ggcccgaaaa	ctaaaaggct	ctggcggtac	gacgtattct	gtacaccctgt	720
gcacagtcca	atctgaactg	gttcggact	catcttcat	gagatggatg	tgtggctt	780
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<210> 333

<211> 3030

<212> DNA

<213> Homo sapien

<400> 333

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gctccatgga	gccggcaat	tatgcccac	tgc	tgatggagc	caaggatatc	gaaggcttgc	180
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cgc	ccaaagca	atgc	ccacca	tgc	ccctgggg	tgc	360
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agtaccc	cc	act	cc	ct	act	cc	540
ctatggccag	ttac	ctgg	ac	gtgt	ctgt	ggact	600
gacatgact	cct	gtt	gg	act	ctcg	ctct	660
acagccagat	gt	tt	gg	tt	ctcg	ctgt	720
ttgcagactc	cag	ccgg	ccag	cac	ct	tcg	780
aacgcattcc	gt	ac	ag	gtt	cc	ggact	840
agttcatcac	ca	agg	aca	ag	tct	cg	900
agattaccat	ct	gg	ttt	ca	gg	cc	960
agaacagcgc	tac	cc	cct	ta	gg	gg	1020
gtcctggg	g	ac	cc	at	gg	gg	1080
ccc	cc	cc	cc	cc	gg	gg	1140
ttgg	tt	cc	cc	cc	gg	gg	1200
cccaa	aa	gg	cc	cc	gg	gg	1260
c	tt	gg	cc	cc	gg	gg	1320
ttt	ca	gg	cc	cc	gg	gg	1380
c	cc	cc	cc	cc	gg	gg	1440
gact	gg	gg	gg	gg	gg	gg	1500
tct	ca	gg	gg	gg	gg	gg	1560
ttt	cc	gg	gg	gg	gg	gg	1620
cc	cc	cc	cc	cc	gg	gg	1680
ggat	cc	cc	cc	cc	gg	gg	1740
tct	cc	gg	gg	gg	gg	gg	1800
ttt	cc	gg	gg	gg	gg	gg	1860
ggat	cc	cc	cc	cc	gg	gg	1920
tct	cc	gg	gg	gg	gg	gg	1980
ttt	cc	gg	gg	gg	gg	gg	2040
gact	cc	cc	cc	cc	gg	gg	2100
agg	cc	cc	cc	cc	gg	gg	2160
ctgg	cc	cc	cc	cc	gg	gg	2220
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gccagctctc	ctagaaaccc	cgcggcgccc	gccgcagcca	agtgttatg	gcccgcggc	2340
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<210> 334
<211> 2417
<212> DNA
<213> Homo sapien

<400> 334

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ggagtttac	ctgtatttgt	ttaatttcaa	caagcctgag	gactagccac	aatgtaccc	120
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gaatgtgcac	cattgaggat	atctaaactt	agatcaattt	cattttccct	ccaagactat	300
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tatgccagat	atatgtaaaa	gcaacctaca	agctctctaa	tcatgtcac	ctaaaagatt	420
cccgggatct	aataggctca	aagaaaacttc	ttctagaaat	ataaaagaga	aaattggatt	480
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<210> 336
 <211> 147
 <212> PRT
 <213> Homo sapien

<400> 336
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 20 25 30
 Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln
 35 40 45
 Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
 50 55 60
 Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
 65 70 75 80
 Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
 85 90 95
 Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala
 100 105 110
 Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn
 115 120 125
 Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro
 130 135 140
 Ala Phe Trp
 145

<210> 337
 <211> 9
 <212> PRT
 <213> Homo sapien

<400> 337
 Ala Leu Thr Gly Phe Thr Phe Ser Ala
 1 5

<210> 338
 <211> 9
 <212> PRT
 <213> Homo sapien

<400> 338
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 1 5

<210> 339
 <211> 318
 <212> PRT
 <213> Homo sapien

<400> 339
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 Leu Tyr Met Ala Ala Pro Gln Ile Arg Lys Met Leu Ser Ser Gly Val

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35	40	45
Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg		
50	55	60
Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu		
65	70	80
Val Ala Lys Glu Ile Gln Thr Thr Gly Asn Gln Gln Val Leu Val		
85	90	95
Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys		
100	105	110
Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala		
115	120	125
Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met		
130	135	140
His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu		
145	150	160
Leu Glu Lys Leu Lys Glu Ser Ala Pro Ser Arg Ile Val Asn Val Ser		
165	170	175
Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly		
180	185	190
Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala		
195	200	205
Asn Ile Leu Phe Thr Gln Glu Leu Ala Arg Arg Leu Lys Gly Ser Gly		
210	215	220
Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val		
225	230	240
Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe		
245	250	255
Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu		
260	265	270
Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His		
275	280	285
Val Ala Trp Val Ser Ala Gln Ala Arg Asn Glu Thr Ile Ala Arg Arg		
290	295	300
Leu Trp Asp Val Ser Cys Asp Leu Leu Gly Leu Pro Ile Asp		
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<211> 483

<212> DNA

<213> Homo sapien

<400> 340

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gctccaaacg tgacatcaact gatgcttcc tcgggggtgc tgatggcccg ctgggtcacg	360
tgctcaatct cgccattcga ctcttgcctcc aaactgtatg aagacacactg actgcacgtt	420
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ctg	483

<210> 341

<211> 344

<212> DNA

<213> Homo sapien

<400> 341
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 gctgccttac aagtattaaa tattttactt ctttccataa agagtagctc aaaatatgca 180
 attaatttaa taatttctga tgatggttt atctgcagta atatgtatat catctattag 240
 aatttactta atgaaaaact gaagagaaca aaatttgtaa ccactagcac ttaagtactc 300
 ctgattctta acattgtctt taatgaccac aagacaacca acag 344

<210> 342
 <211> 592
 <212> DNA
 <213> Homo sapien

<400> 342
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 cctggcaggt aaaccaatgc caagagatg atggaaacca ttggcaagac tttgttgatg 180
 accaggattg gaattttata aaaatattgt tgatgggaag ttgctaaagg gtgaattact 240
 tccctcagaa gagtgtaaag aaaagtctaga gatgtctataa tagcagctat ttaattggc 300
 aagtgcact gtggaaagag ttcctgtgt tgctgaagtt ctgaaggcga gtcaaattca 360
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 cccgtgtctt tatgcaataa atcgctttct tctaaatttc tcctaggctt cattttccaa 480
 agttctctt ggttgtgtat gtctttctg ctttccatta attctataaa atagtatggc 540
 ttcagccacc cactcttcgc cttagctga ccgtgagtct cggctgccgc tg 592

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 <211> 382
 <212> DNA
 <213> Homo sapien

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 agacttcttg attgtcagtc tttgtcacat ccagtgattt ttttgggtt tttcccttt 240
 ctgactgccc aaggggctca gaacccccagc aatcccttcc tttcactacc ttctttttt 300
 ggggtagttg gaaggggactg aaattgtggg gggaaaggtag gaggcacatc aataaagagg 360
 aaaccaccaa gctgaaaaaaaaaa aa 382

<210> 344
 <211> 536
 <212> DNA
 <213> Homo sapien

<400> 344
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 caactaacct gccactaata gttatgtcat ccctcttattt aatcatcatc ctagccctaa 480
 gtctggccta tgagtacta caaaaaggat tagactgagc cgaataacaa aaaaaaa 536

<210> 345
 <211> 251

<212> DNA
 <213> Homo sapien

<400> 345
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 gcgtggcca ggaaataca tcctacactg cccaggagcc agacacattt atgaaacaga 180
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 gtgccatttc c 251

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 <210> 346
 <211> 282
 <212> DNA
 <213> Homo sapien

<220>
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 agggagacta tacctggctc ttgcctaag tgagaggtct tccctcccgc accaaaaaat 180
 agaaaaggctt tctatttac taccccaaggt aggggaagg agagtaactt tgagtctgtg 240
 ggtctcattt cccaaagggtgc cttcaatgct catnaaaacc aa 282

<210> 347
 <211> 201
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(201)
 <223> n = A,T,C or G

<400> 347
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 tctgagactg actggaccca cccagaccca gggcaaagat acatgttacc atatcatctt 180
 tataaagaat ttttttttgt c 201

<210> 348
 <211> 251
 <212> DNA
 <213> Homo sapien

<400> 348
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 aggagacact cccagcatgg aggagggtt atctttcat cctaggtcag gtctacaatg 180
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 gcccctgcctc c 251

<210> 349
 <211> 251
 <212> DNA

<213> Homo sapien

<400> 349

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cagaagggtc tgaactctac gtgttaccag agaacataat gcaattcatg cattccactt	180
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<210> 350

<211> 908

<212> DNA

<213> Homo sapien

<400> 350

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<210> 351

<211> 472

<212> DNA

<213> Homo sapien

<400> 351

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atatactt cgcacatcaat gaactttgtt ttctttactt ccagtaataa agtaggcaca	300
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tcagccccctt ttggcctgt ttgtttgtt aaaaacctaa tctgcttctt gctttctt	420
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<210> 352

<211> 251

<212> DNA

<213> Homo sapien

<400> 352

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caggctcggtt tccgttccat cgttgcattt cacatgcattt tttccaaaca ttgcactac	180
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<210> 353		
<211> 436		
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<400> 353		
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gtatccaaaa gcaaaacagc agatatacaa aattaaagag acagaagata gacattaaca	180	
gataaggcaa ctTatacatt gacaatccaa atccaataca tttaaacatt tggaaatga	240	
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aaataacaaa ggattgagaa tcatgggtc taatgtataa aagaccagg aaacataaaat	720	
atatcaactg cataaaatgt aatgcatgt gaccaagaa ggccccaaag tggcagacaa	780	
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acacgggatg tcag	854	
<210> 355		
<211> 676		
<212> DNA		
<213> Homo sapien		
<400> 355		
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atcccacaagt catacctgga tgcagcgaa ggggcacgg aggcagcagc agccactgg	180	
gacagcatcg ctgtaaaaag cctaccaatg agagctcagt tcaaggcgaa ccaccccttc	240	
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ccctaattcag atggggttga gtaaggctca gagttgcaga tgaggtgcag agacaatcc	360	
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<210> 356		

<211> 574
 <212> DNA
 <213> Homo sapien

<400> 356

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caagcttccc attttagat ctcagtgcct atgagtatct gacacctgtt cctctttca	180
gtctcttagg gaggcttaaa tctgtctcag gtgtgctaag agtgcgcagcc caaggkggtc	240
aaaagtccac aaaactgcag tcttgcgtgg gatagaagc caagcagtgc ctggacagca	300
gagttctttt ctggggcaac agataaccag acaggactct aatcggtc ttattcaaca	360
ttcttcgtc tctgcctaga ctggaaataaa aagccaatct ctctcggtgc acagggaagg	420
agataacaaggc tcgtttacat gtgatagatc taacaaaggc atctaccgaa gtctggcttg	480
gatagacggc acagggagct cttaggtcag cgctgctgg tggaggacat tcctgagtcc	540
agctttgcag ctttgtcga acagtaactt ccca	574

<210> 357

<211> 393
 <212> DNA
 <213> Homo sapien

<400> 357

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aagccacaac caaracttga ttttatcaac aaaaacccct aaatataaac ggsaaaaaag	180
atagatataa ttattccagt ttttttaaaa cttaaaarat attccattgc cgaattaara	240
araarataag ttgttatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa	300
gcataatctg tacaaaaatta aactgtcctt ttggcattt taacaaattt gcaacgktct	360
tttttttctt ttctgtttt ttttttttt tac	393

<210> 358

<211> 630
 <212> DNA
 <213> Homo sapien

<400> 358

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gcatagagta gggaaagctaa tccagcacag ggaggtcaca gagacatccc taaggaagtg	180
gagtttaaac ttagagaagc aagtgcctaa actgaaggat gtgttgaaga agaagggaga	240
gtagaacaat ttgggcagag ggaaccttat agaccctaag gtggaaaggt tcaaagaact	300
gaaagagagc tagaacagct ggagccgttc tccgggtgtaa agaggagtca aagagataag	360
attaaagatg tgaagattaa gatcttggtg gcattcaggg attggcattt ctacaagaaa	420
tcactgaagg gatgtatgtc acattactt tcacttcagg atggccattc taactccagg	480
ggtagactg gacttagttaa gactggaggc aggttagacct cttctaaggc ctgcgatagt	540
gaaagacaaa aataagtggg gaaattcagg ggtatgtaa aatcagtagg acttaatgag	600
caagccagag gttcctccac aacaaccagt	630

<210> 359

<211> 620
 <212> DNA
 <213> Homo sapien

<400> 359

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ctcaccagaa gaataaaagtg ctctgcctgt tattaaaggta ttactgctgg tgaattaaat	180
atggcattcc ccaaggaaa tagagagatt ctctggatt atgttcaata ttatccac	240

aggattaaact gtttaggaa cagatataaa gcttcggcac ggaagagatg gacaaagcac
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 aatgtaaat aaccttataa gaattctgg tcaaataaaa ttctttaag aaaacatcca
 aatgtcattg acttatcaaa tactatctt gcatataacc tatgaaggca aaactaaaca
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<210> 360
 <211> 431
 <212> DNA
 <213> Homo sapien

<400> 360

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 aaaccttctt agctctttag aagtcaaat ccgggggaaat ttattcttgg caatttat
 tggactcctt atgtgagagc agccgctacc cagctggggt ggtggagcga acccgtca
 agtggacatg cagttggaga gctcttggta accacctaga ggaatacaca ggcacatgtg
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 agattcttag t

<210> 361
 <211> 351
 <212> DNA
 <213> Homo sapien

<400> 361

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 ttgggtcttc tggctcttcc ccaagttcc cagccactcg agggagaaat atcgggaggt
 ttgacttctt cggggctt cccgagggt tcaccgttag ccctgcggcc cttagggctg
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<210> 362
 <211> 463
 <212> DNA
 <213> Homo sapien

<400> 362

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 ccccggtcac agaaatgacc aggttgggt tttcaggtg ccagtgtgg gtcagcagct
 cgtaaaggat ttccgcgtcc gtgtcgccagg acagacgtat atacttccct ttcttcccc
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 agttccat ttcactttgg ttgatcttgg tgcctccat gtgcgtggc tggccatagc
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<210> 363
 <211> 653
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc feature

<222> (1)...(653)

<223> n = A,T,C or G

<400> 363

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tgggaggcac	tacgcaagat	gggactgcgt	cctgggggtga	gacatcctct	ccttggagat	180
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ccaaacagcaa	ccccccggaa	gtatgagttc	ctctrgggccc	tccgttctta	ccatgagasc	300
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ntggccctg	gagctggat	gacattgagt	ttgagctgct	gacctggat	gaggaaggag	540
attttggaga	tccntggcc	agaattccat	ttaccttctg	ggccagatac	caccagaatg	600
cccgctccag	attccctca	accttgcog	gtcccattat	tggtcstgg	ggt	653

<210> 364

<211> 401

<212> DNA

<213> Homo sapien

<400> 364

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aaaacaaggt	ggatagatct	agaattgtaa	catttaaga	aaaccatagc	atttgacaga	180
tgagaaagct	caattataga	tgcaaagtta	taactaaact	actatagtag	taaagaaata	240
catttacac	ccttcatata	aatttactat	cttggcttga	ggcactccat	aaaatgtatc	300
acgtgcata	taaatctta	tatttgcata	ggcggtgcac	tagaggactt	ggactgcaac	360
aagtggatgc	gccccaaaatg	aatcttctt	caatagccca	g		401

<210> 365

<211> 356

<212> DNA

<213> Homo sapien

<400> 365

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taccagagca	tcaagtctct	gcagcaggc	attcttgggt	aaagaaatga	cttccacaaa	180
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gactgtcag	atgtgtatag	tacagttga	caagcctggg	tccatacaga	ccgctggaga	300
acattcggca	atgtccctt	tgtagccagt	ttcttcttcg	agctccgg	gagcag	356

<210> 366

<211> 1851

<212> DNA

<213> Homo sapien

<400> 366

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tcacttccctt	taagcctttg	tgactcttcc	tctgtatgtca	gctttaagtc	ttgttctgg	180
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caaattacat	gtgtatgact	agaaacagca	tactctctgg	ccgtcttcc	agatcttgc	300
aagatacatc	aacattttgc	tcaagttagag	ggctgactat	acttgctgat	ccacaacata	360
cagcaagtat	gagagcagtt	cttccatatac	tatccagcgc	atttaaattc	gctttttct	420
tgattaaaaaa	tttaccaact	tgctgtttt	gctcatgtat	accaagtagc	agtgggtgt	480
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cctttgtcag agctgtcctc tttttgtgt caaggacatt aagttgacat cgtctgtcca	720
gcacgagtt tactacttct gaattcccat tgccagaggc cagatgtaga gcagtcctct	780
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tttgacaaaaa tccagcatcc ttgtatttat ttgtgcagtt ctcagaggaa atgcttctaa	1740
cttttccca tttagtatta ttgtggctgt ggcttgcata taggtggttt ttattacttt	1800
aaggatgtc cttctatgc ctgtttgtc gagggttta attctcgatc	1851

<210> 367

<211> 668

<212> DNA

<213> Homo sapien

<400> 367

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accrtataag agcagtgcctt tggccattaa ttatcttgc attrtagaca grttagtgya	180
gagttggatt tccataactca tctggatat ttggatcagt gccatgttcc agcaacattt	240
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cgtctgtcca gcaggagttt tactacttctt gaattcccat tggcagaggc cagatgtaga	540
gcagtcctat gagagtgaga agactttta gaaaattgtt gtgcactagc tacagccata	600
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aaaaaaaaa	668

<210> 368

<211> 1512

<212> DNA

<213> Homo sapien

<400> 368

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ttcaaaacaga ttggaaaccc ggagttaccc ttgtgggtt gaaactgggtt ggttagacgc	180
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gccttcatgg agcccaggtt ccacgtccgt ggagaagatc tggacaagct ccacagagct	660
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aacaagaagg acaagcaaaa gaggactgt ctacatctgg cctctgccaa tggaaattca	780
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aggacagctc tgayaaaggc cgtacaatgc caggaagatg aatgtgcgtt aatgttgctg	900
gaacatggca ctgatccaa tattccagat gagtatggaa ataccactct ractaygt	960
rtctayaatg aagataaaatt aatggccaaa gcactgctct tatayggtc tgatatcgaa	1020
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gaaaacactg aatttgtaaa aggtataact tactatttt caattttcc ctccttaggt	1320
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<210> 369
<211> 1853
<212> DNA
<213> Homo sapien

<400> 369

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cctatgagac taggctttga gaatcaatag atttttttt taagaatctt ttggcttagga	1560
gccccgttc acgcctgtta ttccagcacc ttgagaggct gaggtggca gatcacgaga	1620
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ggagaatggc atgaacccgg gaggtggagg ttgcagtgcg ccgagatccg ccactacact	1800
ccagcctggg tgacagagca agactctgtc tcaaaaaaaaaaaa aaaaaaaaaaaa aaa	1853

<210> 370
<211> 2184
<212> DNA

<213> Homo sapien

<400> 370

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tttcctctga	gaactgcaac	aataaataca	aggatgctgg	attttgtcaa	atgcctttc	180
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tgtagtccca	gctactcagg	argctgaggc	aggagaatgg	catgaacccg	ggaggtggag	2100
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<210> 371

<211> 1855

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1855)

<223> n = A,T,C or G

<400> 371

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gccgcgcgcgc	cataaccgtc	agactggct	gtAAACGGCTT	gcaggcgcac	gccgcacgc	180
cgttaacggct	tggctgcct	gtAAACGGCTT	gcacgtgcac	gtgcacgcgc	cgttaacgc	240
ttggctggca	tgtagccgct	tggctggct	ttgcattt	tgctkggctk	ggcggttgkty	300
tcttggattg	acgtttccctc	cttggatkg	cgtttccctc	ttggatkgac	gtttcytyty	360

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gtaacntgct agttggtaa actgggttgtt agacgctgatc tgctggact actgtttctc	660
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agaagccatt tggtctcagg agcaagatgg gcaagtgggt cgccactgct tcccctgtcg	780
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<210> 372

<211> 1059

<212> DNA

<213> Homo sapien

<400> 372

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gcgcttgrgg agactmcgat gacagygcct tcatggagcc caggtaccac gtccgtggag	180
aagatctgga caagctccac agagctccc tgggtgggtt aagtccccag aaaggatctc	240
atcgctcatgc tcagggacac tgaygtgaac aagarggaca agcaaaagag gactgctcta	300
catctggcct ctgccaatgg gaattcagaa gtagtaaaac tcstgctgga cagacgatgt	360
caacttaatg tccttgacaa caaaaagagg acagctctga yaaaggccgt acaatgccag	420
gaagatgaat gtgcgttaat gttgctggaa catggcactg atccaaatat tccagatgag	480
tatggaaata ccactctrca ctaygctrcc tayaatgaag ataaaattat gccaaagca	540
ctgctttat aygggtgtga tatcgaatca aaaaacaagg tatagatcta ctaattttat	600
cttcaaaaata ctgaaatgca ttcattttaa cattgacgtg tgtaagggcc agtcttcgt	660
atttggaaagc tcaagcataa cttgaatgaa aatattttga aatgacctaa ttatctaaga	720
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aatgcacttc tggtaaatac ttttggtaa aacactgaat ttgtaaaagg taataacttac	840
tatTTTCAA ttttccctc ctaggatTTT ttcccctaa tgaatgtaa atggcaaaat	900
ttgcccgtaa ataggTTTA catgaaaact ccaagaaaag ttaaacatgt ttcaatgtat	960
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<210> 373

<211> 1155

<212> DNA

<213> Homo sapien

<400> 373

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agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag	180
atggcaagt ggtccgcca ctgctccccct tgctgcaggg ggagtggcaa gagcaacgtg	240
ggcgcttcg gagaccacga cgactctgct atgaagacac tcaggaacaa gatggcaag	300
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ggagactacg atgacagtgc cttcatggag cccaggtacc acgtccgtgg agaagatctg	420
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ctcagggaca ctgacgtgaa caagaaggac aagcaaaaaga ggactgctct acatctggcc	540
tctgccaatg ggaattcaga agtagtaaaa ctctctgctgg acagacgtat tcaacttaat	600
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caaaatgata ctcagaagca attttgtgaa gaacagaaca ctgaaatattt acacgatgag	1800
attctgattc atgaagaaaaa gcaagatgaa gttgggtgaaa aaatgaattt tgagcttct	1860
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<210> 374

<211> 2000

<212> DNA

<213> Homo sapien

<400> 374

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agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag	180
atggcaagt ggtccgcca ctgctccccct tgctgcaggg ggagtggcaa gagcaacgtg	240
ggcgcttcg gagaccacga cgactctgct atgaagacac tcaggaacaa gatggcaag	300
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ctcagggaca ctgacgtgaa caagaaggac aagcaaaaaga ggactgctct acatctggcc	540
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attctgattc atgaagaaaaa gcaagatgaa gttgggtgaaa aaatgaattt tgagcttct	1860
cttagttgta agaaagaaaaa agacatcttgc catgaaaata gtacgttgcg ggaagaaaatt	1920

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aaaaaaaaaaa aaaaaaaaaaa	2000

<210> 375
<211> 2040
<212> DNA
<213> Homo sapien

<400> 375

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gtccttgaca acaaaaaaagag gacagctctg ataaaggccg tacaatgcca ggaagatgaa	660
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<210> 376
<211> 329
<212> PRT
<213> Homo sapien

<400> 376

Met Asp Ile Val Val Ser Gly Ser His Pro Leu Trp Val Asp Ser Phe			
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Leu His Leu Ala Gly Ser Asp Leu Leu Ser Arg Ser Leu Met Ala Glu			
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Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser			
35	40	45	
Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg			
50	55	60	

Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
 65 70 75 80
 Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
 85 90 95
 Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
 100 105 110
 His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
 115 120 125
 Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
 130 135 140
 Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
 145 150 155 160
 Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
 165 170 175
 Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
 180 185 190
 Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
 195 200 205
 Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
 210 215 220
 Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
 225 230 235 240
 Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
 245 250 255
 Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
 260 265 270
 Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
 275 280 285
 Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
 290 295 300
 Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
 305 310 315 320
 Ser Met Leu Phe Leu Val Ile Ile Met
 325

<210> 377
 <211> 148
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(148)
 <223> Xaa = Any Amino Acid

<400> 377
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 Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
 20 25 30
 Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
 35 40 45
 Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
 50 55 60
 Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
 65 70 75 80
 Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
 85 90 95

Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
 100 105 110
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
 115 120 125
 Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser
 130 135 140
 Lys Asn Lys Val
 145

<210> 378
 <211> 1719
 <212> PRT
 <213> Homo sapien

<400> 378
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 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His Val

340	345	350
Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile		
355	360	365
Ser Ser Glu Asn Ser Asn Pro Glu Asn Val Ser Arg Thr Arg Asn Lys		
370	375	380
Pro Arg Thr His Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser		
385	390	395
Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys		
405	410	415
Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly		
420	425	430
Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys		
435	440	445
Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly		
450	455	460
Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys		
465	470	475
Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys		
485	490	495
Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp		
500	505	510
Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu		
515	520	525
Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp		
530	535	540
Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln		
545	550	555
Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val		
565	570	575
Val Lys Leu Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn		
580	585	590
Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu		
595	600	605
Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp		
610	615	620
Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys		
625	630	635
Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys		
645	650	655
Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys		
660	665	670
Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala		
675	680	685
Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly		
690	695	700
Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser		
705	710	715
Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser		
725	730	735
His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln		
740	745	750
Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys		
755	760	765
Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser		
770	775	780
Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp		
785	790	795
Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly		800

805	810	815
Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn		
820	825	830
Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe		
835	840	845
Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser		
850	855	860
Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn		
865	870	880
Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu		
885	890	895
Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile		
900	905	910
Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn		
915	920	925
Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro		
930	935	940
Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu		
945	950	960
Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe		
965	970	975
Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His		
980	985	990
Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser		
995	1000	1005
Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu		
1010	1015	1020
Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His		
1025	1030	1040
Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met		
1045	1050	1055
Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met		
1060	1065	1070
Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys		
1075	1080	1085
Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr		
1090	1095	1100
Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys		
1105	1110	1120
Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp		
1125	1130	1135
Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His		
1140	1145	1150
Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp		
1155	1160	1165
Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg		
1170	1175	1180
Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val		
1185	1190	1200
Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys		
1205	1210	1215
Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly		
1220	1225	1230
Asn Ser Glu Val Val Lys Leu Leu Asp Arg Arg Cys Gln Leu Asn		
1235	1240	1245
Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys		
1250	1255	1260
Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro		

1265	1270	1275	1280
Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr	Leu His Tyr Ala Ile Tyr		
1285	1290	1295	
Asn Glu Asp Lys Leu Met Ala Lys Ala	Leu Leu Leu Tyr Gly Ala Asp		
1300	1305	1310	
Ile Glu Ser Lys Asn Lys His Gly	Leu Thr Pro Leu Leu Leu Gly Val		
1315	1320	1325	
His Glu Gln Lys Gln Gln Val Val Lys Phe	Leu Ile Lys Lys Lys Ala		
1330	1335	1340	
Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg	Thr Ala Leu Ile Leu Ala		
1345	1350	1355	1360
Val Cys Cys Gly Ser Ala Ser Ile Val Ser	Leu Leu Leu Glu Gln Asn		
1365	1370	1375	
Ile Asp Val Ser Ser Gln Asp Leu Ser Gly	Gln Thr Ala Arg Glu Tyr		
1380	1385	1390	
Ala Val Ser Ser His His His Val Ile Cys	Gln Leu Leu Ser Asp Tyr		
1395	1400	1405	
Lys Glu Lys Gln Met Leu Lys Ile Ser Ser	Glu Asn Ser Asn Pro Glu		
1410	1415	1420	
Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu	Ser Gln Arg Phe Lys Gly		
1425	1430	1435	1440
Ser Glu Asn Ser Gln Pro Glu Lys Met Ser	Gln Glu Pro Glu Ile Asn		
1445	1450	1455	
Lys Asp Gly Asp Arg Glu Val Glu Glu Met	Lys Lys His Glu Ser		
1460	1465	1470	
Asn Asn Val Gly Leu Leu Glu Asn Leu Thr	Asn Gly Val Thr Ala Gly		
1475	1480	1485	
Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg	Lys Ser Arg Thr Pro Glu		
1490	1495	1500	
Asn Gln Gln Phe Pro Asp Asn Glu Ser	Glu Tyr His Arg Ile Cys		
1505	1510	1515	1520
Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln	Met Pro Lys Tyr Ser Ser		
1525	1530	1535	
Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys	Leu Thr Ser Glu Glu Glu		
1540	1545	1550	
Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly	Gln Pro Glu Lys Arg Ser		
1555	1560	1565	
Gln Glu Pro Glu Ile Asn Lys Asp Gly	Asp Arg Glu Leu Glu Asn Phe		
1570	1575	1580	
Met Ala Ile Glu Glu Met Lys Lys His	Gly Ser Thr His Val Gly Phe		
1585	1590	1595	1600
Pro Glu Asn Leu Thr Asn Gly Ala Thr	Ala Gly Asn Gly Asp Asp Gly		
1605	1610	1615	
Leu Ile Pro Pro Arg Lys Ser Arg Thr	Pro Glu Ser Gln Gln Phe Pro		
1620	1625	1630	
Asp Thr Glu Asn Glu Glu Tyr His Ser Asp	Glu Gln Asn Asp Thr Gln		
1635	1640	1645	
Lys Gln Phe Cys Glu Glu Gln Asn Thr	Gly Ile Leu His Asp Glu Ile		
1650	1655	1660	
Leu Ile His Glu Glu Lys Gln Ile Glu Val	Val Glu Lys Met Asn Ser		
1665	1670	1675	1680
Glu Leu Ser Leu Ser Cys Lys Lys Glu	Lys Asp Ile Leu His Glu Asn		
1685	1690	1695	
Ser Thr Leu Arg Glu Glu Ile Ala Met	Leu Arg Leu Glu Leu Asp Thr		
1700	1705	1710	
Met Lys His Gln Ser Gln Leu			
1715			

<210> 379
 <211> 656
 <212> PRT
 <213> Homo sapien

<400> 379
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
 340 345 350
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
 355 360 365
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
 370 375 380
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
 385 390 395 400
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
 405 410 415

Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
 420 425 430
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
 435 440 445
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
 450 455 460
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
 465 470 475 480
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
 485 490 495
 Leu Lys Leu Thr Ser Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
 500 505 510
 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
 515 520 525
 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
 530 535 540
 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
 545 550 555 560
 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
 565 570 575
 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
 580 585 590
 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
 595 600 605
 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
 610 615 620
 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
 625 630 635 640
 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
 645 650 655

<210> 380
 <211> 671
 <212> PRT
 <213> Homo sapien

<400> 380
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala

165	170	175
Leu His Leu Ala Ser Ala Asn Gly Asn Ser	Glu Val Val Lys	Leu Leu
180	185	190
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn	Lys Lys Arg Thr	
195	200	205
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp	Glu Cys Ala Leu Met	
210	215	220
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro	Asp Glu Tyr Gly Asn	
225	230	235
240		
Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp	Lys Leu Met Ala Lys	
245	250	255
Ala Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn	Lys His Gly	
260	265	270
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys	Gln Gln Val Val	
275	280	285
Lys Phe Leu Ile Lys Lys Ala Asn Leu Asn Ala Leu	Asp Arg Tyr	
290	295	300
Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys	Gly Ser Ala Ser Ile	
305	310	315
320		
Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser	Ser Gln Asp Leu	
325	330	335
Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser	His His His Val	
340	345	350
Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys	Gln Met Leu Lys Ile	
355	360	365
Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu	Lys Leu Thr Ser Glu	
370	375	380
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn	Ser Gln Pro Glu Lys	
385	390	395
400		
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly	Asp Arg Glu Val Glu	
405	410	415
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val	Gly Leu Leu Glu Asn	
420	425	430
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp	Asn Gly Leu Ile Pro	
435	440	445
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln	Phe Pro Asp Asn Glu	
450	455	460
Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val	Ser Asp Tyr Lys Glu	
465	470	475
480		
Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser	Asn Pro Glu Gln Asp	
485	490	495
Leu Lys Leu Thr Ser Glu Glu Ser Gln Arg	Leu Glu Gly Ser Glu	
500	505	510
Asn Gly Gln Pro Glu Lys Arg Ser Gln Glu Pro	Glu Ile Asn Lys Asp	
515	520	525
Gly Asp Arg Glu Leu Glu Asn Phe Met Ala Ile	Glu Met Lys Lys	
530	535	540
His Gly Ser Thr His Val Gly Phe Pro Glu Asn	Leu Thr Asn Gly Ala	
545	550	555
560		
Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro	Pro Arg Lys Ser Arg	
565	570	575
Thr Pro Glu Ser Gln Gln Phe Pro Asp	Thr Glu Asn Glu Glu	Tyr His
580	585	590
Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe	Cys Glu Glu Gln Asn	
595	600	605
Thr Gly Ile Leu His Asp Glu Ile Leu Ile His	Glu Glu Lys Gln Ile	
610	615	620
Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser	Cys Lys Lys	

625	630	635	640												
Glu	Lys	Asp	Ile	Leu	His	Glu	Asn	Ser	Thr	Leu	Arg	Glu	Glu	Ile	Ala
645	650	655													
Met	Leu	Arg	Leu	Glu	Leu	Asp	Thr	Met	Lys	His	Gln	Ser	Gln	Leu	
660	665	670													

<210> 381
<211> 251
<212> DNA
<213> Homo sapien

<400> 381

ggagaagcgt	ctgctggggc	aggaaggggt	tccctgccc	tctcacctgt	ccctcaccaa	60
ggttaacatgc	ttccccctaag	ggtatccaa	cccagggggc	tcaccatgac	ctctgagggg	120
ccaatatccc	aggagaagca	ttggggagtt	ggggcaggt	gaaggaccca	gactcacac	180
atcctgggcc	tccaaggcag	aggagagggt	cctcaagaag	gtcaggagga	aatccgtaa	240
caagcagtca	g					251

<210> 382
<211> 3279
<212> DNA
<213> Homo sapiens

<400> 382

cttcctgcag	ccccatgt	ggtgaggggc	acgggcagga	acagtggacc	caacatggaa	60
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caactggagg	ggacatcctg	cagaaggtag	gagttagca	acacccctg	caggggaggg	180
gagagccctg	cggcacctgg	gggagcagag	ggagcagcac	ctgcccaggc	ctgggaggag	240
gggcctggag	ggcgtgagga	ggagcggagg	ggctgcatgg	ctggagtgag	ggatcagggg	300
caggcgcgca	gatggcctca	cacagggaaag	agagggccccc	tcctgcaggg	cctcacctgg	360
gccacaggag	gacactgctt	ttccctctgag	gagtcaggag	ctgtggatgg	tgctggacag	420
aagaaggaca	gggcctggct	caggtgtcca	gaggctgtcg	ctggcttccc	tttggatca	480
gactgcaggg	agggagggcg	gcagggttgt	ggggggagtg	acgatgagga	tgacctgggg	540
gtggctccag	gccttgc	tgccctggcc	ctcacccagc	ctccctcaca	gtctcctggc	600
cctcagtc	tcccctccac	tccatccccc	atctggc	agtgggtcat	tctgatca	660
gaactgacca	tacccagccc	tgcccacggc	cctccatggc	tcccaatgc	cctggagagg	720
ggacatctag	tca	gagatggat	gtcc	ggcgttgc	tgtggggca	780
gcatctgc	gatggtccc	gcctcata	tgctgac	tctgcaggg	ctgtcctc	840
ggaccttgcc	ccttgcag	gagctggacc	ctgaagtccc	ctccccatag	gccaagactg	900
gagccttgtt	ccctctgtt	gactccctgc	ccatattctt	gtgggagtgg	gttctggaga	960
catttctgtc	tgttctgag	agctggaaat	tgctctc	catctgc	cgcggttctg	1020
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gcattacccg	aagtggatca	aggacaccat	cgcagccaa	ccctgagtg	ccctgtccca	1260
cccttaccc	tagaaattt	aagtccac	cacgttctgg	catca	ccttctgg	1320
tgctggacac	ctgaagctt	gaactcac	ggccga	cgagc	cct	1380
gacctgtct	ttctgggt	gagttcc	gggg	gag	ctact	1440
tgtatgc	ttttctgaa	atgggtataa	tttgc	tcctt	ggaa	1500
ctctgaagac	ttctcg	gtttc	ggac	cac	actgtgt	1560
tgttctgg	gtc	gag	gggg	aa	gtgaccatgt	1620
caagggtggac	actctctaca	gatc	gggg	ag	gtgac	1680
acacacagca	agttgac	tgt	gggg	cc	ggc	1740
ctagataagg	ccgtg	agg	gggg	act	gggaa	1800
tagggggaga	aactgaa	ttt	gggg	gg	gggac	1860
cgtcagatt	gtgatttcc	tagc	gggg	ttt	gggg	1920
ttattatgtt	ttgttacatt	gat	gggg	ata	ttt	gggg
tagatttag	tgtggagaaa	acag	gggg	ttt	gggg	1980
						2040

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gtagctgatc cagctgatag aggaacttagc caggtgggg ctttccctt tggatgggg 2160
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atcattgtt tatttgcctt ctttcacac cattggtag ggagggatta ccaccctggg 2820
gttatgaaga tgggtgaaca ccccacacat acacccggag atatgagatc aacagtttct 2880
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acaagacggt ggggcaaact ctgattccg tggggaaatg tcatggtctt gctttactaa 3060
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cccagctgat agaggaagta gccaggtggg agccttccc agtgggtgtg ggacatatact 3180
ggcaagattt tggcactc ctggttacag atactggggc agcaaataaa actgaatctt 3240
gttttcagac cttaaaaaaaa aaaaaaaaaa aaaatgtttt 3279

<210> 383

<211> 154

<212> PRT

<213> Homo sapiens

<400> 383

Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
5 10 15

Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
20 25 30

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
50 55 60

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
65 70 75 80

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
85 90 95

Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
 100 105 110

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
115 120 125

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
 130 135 140

Ala Leu Glu Arg Gly His Leu Val Arg Glu
145 150

<210> 384
<211> 557
<212> DNA
<213> Homo sapiens

<400> 384
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aaagatgtgt ttgtttgg actctctgtg gtcccttcca atgctgtggg tttccaacca 120
ggggaaagggt ccctttgca ttgccaagtg ccataaccat gagcactact ctaccatgg 180
tctgcctctt gccaaggcag gctggtttc aagaatgaaa tgaatgatt tacagctagg 240
acttaaccc ttgaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300
ctctgttagag agcagcatc ccagggaccc tggaaacagt tggactgtt aggtgcttgc 360
-tcccccaagac acatcctaaa aggtgttgc atggtaaaaa cgtcttccctt ctttattgcc 420
ccttcttatt tatgtgaaca actgtttgtc ttttttgc tctttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttc aaagtaaaaa 540
aaaaaaaaaaa aaaaaaaaaa 557

<210> 385
<211> 337
<212> DNA
<213> Homo sapiens

<400> 385
ttcccaggtg atgtgcgagg gaagacacat ttactatcc ttagtgggct gattccttta 60
gtttctctag cagcagatgg gtttaggagga agtgcacccaa gtgggttact cctatgtca 120
tctcaaagcc atctgtgtc tttagtgcg gacacatcat cactcctgca ttgttgcata 180
aaacgtggag gtgttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtccagtttcc cgccaccaaca cctgtgtgtt ccctgtcgtg gtctggatct 300
cttggccac caattcccc tttccacat cccggca 337

<210> 386
<211> 300
<212> DNA
<213> Homo sapiens

<400> 386
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gccccgctcg cccagagggt gggcgccggg ctgcctctac cggctggcgg ctgttaactca 120
gcgcacccctgg cccgaaggct ctagcaagga cccaccgacc ccagccgcgg cgccggccgc 180
gcggactttg cccgggtgtt ggggcggagc ggactgcgtg tccgcggacg ggcagcgaag 240
atgttagct tcgctgccag gaccgtggac cgatcccagg gctgtgggtt aacctcagcc 300

<210> 387
<211> 537
<212> DNA
<213> Homo sapiens

<400> 387
ggcccgagtc gggcaccaag ggactcttg caggcttcct tcctcgatc atcaaggctg 60
ccccctctg tgccatcatg atcagcacct atgagttcg caaaagcttc ttccagaggc 120
tgaaccagga ccggcttctg ggcggctgaa agggcaagg aggcaaggac cccgtctctc 180
ccacggatgg ggagaggcga ggaggagacc cagccaagtg cttttccctc agcaactgagg 240
gagggggctt gtttccctc cctcccgccg acaagctcca gggcagggtt gtcctctgg 300
gcggcccccagc acttccctcag acacaacttc ttccgtctgc tccagtctgt gggatcatca 360
cttacccacc ccccaagttc aagaccaaat cttccagctg ccccttcgt gttccctgt 420
gtttgtgtt gctggccatg tttccagaa ccaagaagcc ctcagctgg ttttgtctcc 480
ctgacccttg ttaattccctt aagtctaaag atgatgaact taaaaaaaaaaa aaaaaaaaaa 537

<210> 388
<211> 520
<212> DNA
<213> Homo sapiens

<400> 388
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gtttaagat tgcttcttct acagttctg agaattgtgt tatttcactt gccaagtgaa 180
ggacccttc cccaaacatgc cccagccccac ccctaagcat ggtcccttgt caccaggcaa 240
ccaggaaact gctacttgtg gacccacca gagaccagga gggtttgggtt agctcacagg 300
acttccccca ccccagaaga ttagcatccc atactagact catactcaac tcaacttaggc 360
tcatactcaa ttgatggta ttagacaatt ccatttctt ctggtttatta taaacagaaa 420
atcttcttc ttctcattac cagtaaaggc tcctggatc tttctgttgg aatgatttct 480
atgaacttgt cttatTTAA tggtgggtt ttttctgg 520

<210> 389
<211> 365
<212> DNA
<213> Homo sapiens

<400> 389
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gagtttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgcct ctgcgtcccc 120
aacgacttcc caaataatct caccagcgcc ttccagctca ggcgtccctag aagcgtctt 180
aaggctatgg ccagctgtct ttgtgttccc ttcacccgc ctgtccctcac agctgagact 240
cccaggaaac cttcagacta cttccctctg cttcagcaa ggggcgttgc ccacattctc 300
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gggag 365

<210> 390
<211> 221
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(221)
<223> n = A,T,C or G

<400> 390
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tacacggntt ctcatgggtg tggAACATCT ctgttgcgg ttccagaag gcctctggct 120
gctctangag tctganncga ntctggccc cantntgaca naaggaaagg cgagcttat 180
tcaaaagtcta gaggagtgaa aggagttaa gctggatttc a 221

<210> 391
<211> 325
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(325)
<223> n = A,T,C or G

<400> 391

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 ctctcgccc cagcctggag ctgcctctgg catctaccaa caatcagncc aggcgagcag 120
 tagccaggc actgctgcc aacgcgcgtc cnataccat catgtncatcc ggtngctct 180
 naantngat ntccanagcc ctacccatcn tagttctgct ctccccccgg ntaccagccc 240
 cactgcccag gaatctaca gccagtaccc tgtcccgacg tctctaccta ccagtacgt 300
 gagacccctcg gctactacta tgacc 325

<210> 392

<211> 277

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(277)

<223> n = A,T,C or G

<400> 392

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 antaccanga accgnatgn cttanaaanc ncctggttt tgggtnntc aatgactgca 180
 tgcagtgcac caccctgtcc actacgtat gctgttagat taaagtctca cagtggcgg 240
 ctgaggatac agcgcycgt cctgtgtgc tgggaa 277

<210> 393

<211> 566

<212> DNA

<213> Homo sapiens

<400> 393

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 gtatctaca ttctgaagtt gtctgaaaat gtcttcatga taaaattcag cctaaacgtt 120
 ttgcgggaa cactgcagag acaatgtgt gagttccaa ccttagccca tctgcggca 180
 gagaaggctt agtttgtcca tcagcattat catgatatca ggactggta cttggtaag 240
 gaggggtcta ggagatctgt ccctttaga gacacccatc ttataatgaa gtattggaa 300
 ggggtgttt caaaagtata aatgtccgtt attccgatga tcatcctgtt aacatttat 360
 catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
 ttctgcctca atgtttactg tgccttgc tttctgtt tttctgtt aaaaaaaaaa 480
 cattctctgc ctgagttta atttttgtcc aaagtttattt taatctatac aattaaaage 540
 ttttgcctat caaaaaaaaaaaaaa 566

<210> 394

<211> 384

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(384)

<223> n = A,T,C or G

<400> 394

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 tgcaaattng gacccggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
 gcaggaggac cgggtttaa ggagtttaa gctgagtgcc actgttagacc ccaaatacca 180
 tcccaagatt atcggggagaa agggggcagt aattacccaa atccgggtgg agcatgacgt 240
 gaacatccag tttcctgata aggacgtgg gaaccagccc caggaccaaa ttaccatcac 300
 agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360

<pre> tgagcagatg gtttctgagg acgt <210> 395 <211> 399 <212> DNA <213> Homo sapiens <400> 395 ggcaaaactg tggacacta ataagaccc gcatccaa ggtcaagtat cagaagtgcac 60 tctgaccctt gactccaaga cctacatcaa cagcctggct atatttagatg atgagccagt 120 tatcgaggt ttcatcattt cgaaaattgt ggagtctaag gaaatcatgg cctctgaagt 180 attcacgtct ttccagtacc ctgagttctc tatagagttt cctaacacag gcagaattgg 240 ccagctactt gtctgcaatt gatatcttcaa gaataccctg gccatccctt tgactgacgt 300 caagttctct ttggaaagcc tggcatctc ctcactacag acctctgacc atgggacgg 360 gcagcctggc gagaccatcc aatccaaat aaaatgcac 399 <210> 396 <211> 403 <212> DNA <213> Homo sapiens <220> <221> misc_feature <222> (1)...(403) <223> n = A,T,C or G <400> 396 tggagttntc agtgcaaaca agccataaaag cttcagtagc aaattactgt ctcacagaaa 60 gacattttca acttctgtcc cagctgtca taaaacaaat catgtgtta gcttgactcc 120 agacaaggac aacctgttcc ttcat'aactc tcttagagaaa aaaaggagtt gttagtagat 180 actaaaaaaa gtggatgaat aatctggata ttttcctaa aaagattcct taaaacacat 240 taggaaaatg gaggccctt tgatcagaat gctagaatta gtccatgtg ctgaaggcagg 300 gttttagggg gggagtgagg gataaaagaa ggaaaaaaaaag aagagtgaga aaacctattt 360 atcaaagcag gtgttatcac tcaatgttag gccctgtct ttt 403 <210> 397 <211> 100 <212> DNA <213> Homo sapiens <220> <221> misc_feature <222> (1)...(100) <223> n = A,T,C or G <400> 397 actagtnca gttgtggaa ttgcggccg cgtcgaccta naanccatct ctatagcaaa 60 tccatccccg ctctggttt gtnacagaat gactgacaaa 100 <210> 398 <211> 278 <212> DNA <213> Homo sapiens <220> <221> misc_feature <222> (1)...(278) <223> n = A,T,C or G </pre>	384
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ccacctggac atctggaaat cagcggcctg gatgaaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgagggtgg actcatcatg 180
ctccgggcag cccatccacc tgtggcagtt cctaaggag ttgctactca agccccacag 240
ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

<210> 399
<211> 298
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(298)
<223> n = A,T,C or G

<400> 399
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gggggtgcnc catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtggc 120
ccgagatcga ggcgcattggc ctggatcatgg accgcattggg ctccgtggag cgcattggc 180
ccggcatcga ggcgcattggc cgcgcattggc tcgaccacat ggcctccanc attgancgca 240
tggccagac catggagcgc attggctctg gggtggagcn catgggtgcc ggcattggg 298

<210> 400
<211> 548
<212> DNA
<213> Homo sapiens

<400> 400
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gtacatgtac atgtatgaaa ttcccttctc ttaccgaact ctctccacac atcacaagg 120
caaagaacca cacgcttaga aggtaagag ggcaccctat gaaatgaaat ggtgatttct 180
tgagtctt tttccacgt ttaagggcc atggcaggac tttagattgc gagttaaagac 240
tgcagaggc tagagaatta ttccatacag gcttggagc caccatgtc acttaccccg 300
tataccctt caccatcccc ttgtctactc tgatgcccc aagatgcaac tggcagacta 360
gttggccca taattctggg ctttgggtt ttgttttaat tacttggca tcccaggaag 420
ctttccagtg atctcctacc atggggccccc ctccctggat caagccctc ccaggccctg 480
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agcaggtt 548

<210> 401
<211> 355
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(355)
<223> n = A,T,C or G

<400> 401
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ttagtgcctcc aagtatgttcca ctttcattttt actctttgaa actgtatcat ctccctggaa 120
taagatgtgtt ggccttatttcc agctgcatttgc acaaaaatgtac tggctcttgc cttaaacgttc 180
tataaatgaa ttttgttgcacca ttttgttgcacca ttttgttgcacca ttttgttgcacca 240
tttttgttgcacca ttttgttgcacca ttttgttgcacca ttttgttgcacca ttttgttgcacca 300

ccctttgca ttgccaaagtg ccataaccat gagcactact ctaccatggc tctgc 355
<210> 402
<211> 407
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(407)
<223> n = A,T,C or G

<400> 402
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tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaaag caggtgttc actccctactt tctgacaaaaa cagactatgc 180
gaataaaagat aaaaaagaga aggacattac aaaggtggtc ctgaccttg ataaaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctcccctgc agagagttcc tgatctccca aaatttggtt gagatgtaaag 360
gntgattttg ctgacaactc ctttctgaa gtttactca tttccaa 407

<210> 403
<211> 303
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

<400> 403
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tcctaagcaa gagccatggc atggtaaaaa tgccaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcataaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgttaatta tagagcgaga agatgacagt gatctgttcc tggcacaaca 240
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
gga 303

<210> 404
<211> 225
<212> DNA
<213> Homo sapiens

<400> 404
aagtgttaact tttaaaaatt tagtgattt tgaaaattct tagagggaaag taaaaggaaaa 60
attgttaatg cactcattt cctttacatg gtggaaagtgc tctcttgatc ctacaaacag 120
acattttcca ctctgtttc catagttgtt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaaagtgc ctgtgtataa aataaagtat ctttatttca ttcat 225

<210> 405
<211> 334
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(334)

<223> n = A,T,C or G

<400> 405

gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgagggttg tctggaggac 60
ttcaatacac ctcffffccat agtgaatcag cttccagggg gtccagtccc ttccttact 120
tcatccccat cccatgccaa aggaagaccc tccctccttg gctcacagcc ttctctaggc 180
ttcccagtgc ctcaggaca gagtgggta tgtttcage tccatccttg ctgtgagtgt 240
ctggtcgggt tgcctcca gcttctgtc agtgcattcat ggacagtgtc cagccatgt 300
cactctccac tctctcanng tggatccac ccct 334

<210> 406

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(216)

<223> n = A,T,C or G

<400> 406

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gaaaacaaca cccaaataaac tggagtgcc agactgacaa ctgtgagaca tgcacttgt 120
acnaaacaaca aattnatgt tgcacccttg tttctacacc tgtgggat gacaaagaca 180
actgccaag aatnttcaag aaggaggact gccant 216

<210> 407

<211> 413

<212> DNA

<213> Homo sapiens

<400> 407

gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcattgc cttgactcat 60
gtaaatgca taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatattt 120
gtacaacatt gcacccagtgc tcagattcta caccggcca ctcaggaagc aagagttat 180
cccaggggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaatgtt catttgtcca tgtgacagtt gatacttattt cacatttcattt atgggcaacc 300
tgccagacag gagaaaagtct tcccatgtta aaagacattt attatcttgtt tttctgtca 360
tgggagttcc agaaaaagtt aaaacagaca atggggcagg ttctgttagta aag 413

<210> 408

<211> 183

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(183)

<223> n = A,T,C or G

<400> 408

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tncttaacta gttaatcctt aaagggtctt ntaatccttta actagtccctt ccattgtgag 120
cattatcctt ccagtattcn cttctnttt tatttactcc ttctggcta cccatgtact 180
ntt 183

<210> 409

<211> 250

<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(250)
<223> n = A,T,C or G

<400> 409
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gtggtttggg ggacctgaac aaacctcctt taattaatca gctttcagtt tctcccccta 120
gtccccctt caacaacata ggaggatcct ccccttctt ctgctcacgg ccttatctag 180
gcttcccagt gcccccaagga cagcgtggc tatgtttaca ggcgcntcctt gctggggggg 240
250
ggccntatgc

<210> 410
<211> 306
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(306)
<223> n = A,T,C or G

<400> 410
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agtcttgcaa tcccatttgc aggatccgtc tgtgcacatg cctctgtaga gagcagcatt 120
cccaggacc ttggaaacag ttggcactgt aaggtgcttgc ctccccaaaga cacatcctaa 180
aaggtgttgtt aatggtaaaa accgcttctt tctttattgc cccttcttat ttatgtgaac 240
nactgggttgg cttttttgn atctttttta aactggaaag ttcaatttngaaaatgaata 300
306
tcntgc

<210> 411
<211> 261
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(261)
<223> n = A,T,C or G

<400> 411
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ggatcttttgc tatttaagga ttctgagatt ttgcttgagc aggatttagat aaggctgttc 120
tttaaatgtc taaaatggaa cagattcaa aaaaaaaccacacaatcttag ggtggaaaca 180
aggaaggaaa gatgtgaata ggctgtatggg caaaaaaaaacca atttacccat cagttccagc 240
261
cttctctcaa ggngaggcaa a

<210> 412
<211> 241
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(241)

<223> n = A,T,C or G

<400> 412

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ggaacatacc agctgaaatt tggaaaaaat aattgtgttt ctgcaggaaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tgaggggag 180
ctgggagatt tcactggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
a 241

<210> 413

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 413

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ctcatccaaag ttcttagtac cttcttttg ttgtgaagga taatcaaact gaacaacaaa 120
aagttactc tcctcatttg gaacctaaaaa actctttct tcctgggtct gagggctcca 180
agaatccttg aatcanttct cagatcatttggggacaccan atcaggaacc t 231

<210> 414

<211> 234

<212> DNA

<213> Homo sapiens

<400> 414

actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggt cttccttgg catggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaaagctga ttcaactatgg gggaggtgt attgaagtcc tcca 234

<210> 415

<211> 217

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(217)

<223> n = A,T,C or G

<400> 415

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caaaaacacag accaggtgc aaatctccac tgctctaagg ntctcaccac cactttctca 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc 217

<210> 416

<211> 213

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature
<222> (1)...(213)
<223> n = A,T,C or G

<400> 416
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ggcacagcag taaaagcttt tgattcccaag aatcaagaac tctcccttc agactattac 120
cgaatgeaag gtggtaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggAAC agatggagtc tctactacaa aag 213

<210> 417
<211> 303
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

<400> 417
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gtggaaagg cttactctg agttcaatc ttcaagccca tcagagagtc cacactggag 120
agaaggccata caaatgcaat gagtggttggaa agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggccacaca ggagagaaac cctataaatg tgagatatgt ggaaaggcgt 240
tcantcaaag ttcttatctt caaatccatc nagaaggncatc cagttananaa aacctttt 300
agt 303

<210> 418
<211> 328
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

<400> 418
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tgcacaggca tgatctcggc tcactacaac ccctgcctcc catgtccaag cgattcttgt 120
gcctcagccct ccctgttagc tagaattaca ggacatgcc accacacccca gctagtttt 180
gtatTTTtag tagagacagg gttcaccat gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctggtctc aaactcctga cctcaagtga tctgccacc tcagcctccc 300
aaagtctan gattacaggc cgtgagcc 328

<210> 419
<211> 389
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

<400> 419
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acccctgagc catggactgg agcctgaaaag gcagcgatca ccctgtccct gatcttgcgtg 120
cttgtttccct ctctgtggct ccattcatag cacagttgtt gcactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggc gtgccaggca 240
ccggttctcc agccaccaac ctcaactcgct cccgcaaatg gcacatcagt tcttctacc 300
taaaggtagg accaaaggc atctgcttt ctgaagtccct ctgctctatc agccatcacg 360
tggcagccac tcnggctgtc tcgacgcgg 389

<210> 420

<211> 408

<212> DNA

<213> Homo sapiens

<400> 420

gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccaggc agcaaggcctt agccttggct tcttggttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagttt tgactttgggt gtttcggcat ggagaccgaa 180
gtcccatgta caccttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctggc atggagcagc attatgaact tggagagttataaagaaga 300
gatataaaaaa attcttgaat gagtcctata aacatgaaca gtttatattt cgaagcacag 360
acgttgaccg gactttgatg aagtgtatg acaaacctgg caagcccg 408

<210> 421

<211> 352

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(352)

<223> n = A,T,C or G

<400> 421

gctcaaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggccctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcaactgaca gaacaggctt ttttgggtc ctttctcc accacnataat acttgcagtc 180
ctccttcttg aagattctt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240
ggtgcaacat gaaatttctg tttcgttagca agtgcattgtc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtt tttgttccct ttgagatcca tgcatttcct gg 352

<210> 422

<211> 337

<212> DNA

<213> Homo sapiens

<400> 422

atgccaccat gctggcaatg cagccccgg tcgaaggccct gcataatccag cccaaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtaagg 120
gcgatagcaa ggtgcggcg atcgcggcg cgtaatccct ggccaaaggc agccgtgatc 180
gtgaaatggc agtgcgtgaa ttgatctacc cggttatgg catcggcggg cataaggct 240
atccgacacc ggtgcacctg gaagcctgc agccgctggg gccgacgccc attcaccgac 300
gcttcttcccg ccggtaacggc tggcctatga aaattat 337

<210> 423

<211> 310

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature
<222> (1)...(310)
<223> n = A,T,C or G

<400> 423
gctaaaaat cttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgcttactan aagcncatta gattatccat 120
tcactgacag aacaggctt tttgggtcc ttcttctcca ccacgatata ctgcagtcc 180
tccttcttga agattcttg gcagttgtct ttgtcataac ccacaggtgt anaaacaagg 240
gtgcaacatg aaatttctgt ttcgttagcaa gtgcattgtct cacagttgtc aagtctgccc 300
tccgagttta 310

<210> 424
<211> 370
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(370)
<223> n = A,T,C or G

<400> 424
gctaaaaat cttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
caactgacaga acaggtctt tttgggtcc ttcttctccac cacgatatac ttgcagtcc 180
ccttcttga gattcttgg cagttgtctt tgtcataacc cacaggtgt aaaaacatcc 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgtcat tgcataaaagt 300
cacgaaggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
tccgtcagc 370

<210> 425
<211> 216
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

<400> 425
aattgctatn ntttattttg ccactaaaa taattacca aaaaaaaaaa nttaaatga 60
taacaacna acatcaaggn aaananaaca ggaatggntg actntgcata aatnggccga 120
anattatcca ttatnttaag ggttgacttc aggntacagc acacagacaa acatgcccag 180
gaggntntca ggaccgctcg atgtntntg aggagg 216

<210> 426
<211> 596
<212> DNA
<213> Homo sapiens

<400> 426
cttccagtga ggataaccct gttccccgg gccgagggtc tccattagc tctgattgtat 60
tggcagtcag tcatggagg gtgttctgtat cattccgact gcccccaaggg tcgctggcca 120
gctctcttgg ttgtcgatgtt ggcagtagga cctaattgt taattaagag tagatggta 180
gctgtcccttgc tattttgatt aacctaattgg ccttcccagc acgactcgaa ttcagctgg 240
gacatcacgg caactttaa tgaaatgatt tgaaggccca ttaagaggca cttcccgta 300

ttaggcagtt catctgact gataacttct tggcagctga gctggtcgga gctgtggccc 360
 aaacgcacac ttgcgtttg gtttgagat acaactctta atcttttagt catgctttag 420
 ggtggatggc ctttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480
 atacactcat atactcgtagg gcttagaggc cacagcagat gtcattggc tactgcctga 540
 gtcccgctgg tcccatcccc ggaccttcca tcggcgagta cctgggagcc cgtgct 596

<210> 427
<211> 107
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(107)
<223> n = A,T,C or G

<400> 427
gaagaattca agtttagttt attcaaaggc cttacngaga atcctanacc caggncccag 60
ccggggagca gccttanaga gctcctgttt gactgcccgg ctcagng 107

<210> 428
<211> 38
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(38)
<223> n = A,T,C or G

<400> 428
gaacttccna anaangactt tattcaactat tttacatt 38

<210> 429
<211> 544
<212> DNA
<213> Homo sapiens

<400> 429
ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccc 120
atatccacga actcttgaag gactttctga tttatccaca atcaaatcat cggttttcag 180
tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcggt 240
gccttccact tcagttacac ctcactcacc atccctctt gttggttctg tgctgcttca 300
agatactaag cccacattt agatgcagca gccatctccc ccaattccctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgcccttta tgatgtctt gatgttctca tcaagccac 420
gagtttagtt caaagcagta ttcaagcatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gtttagagaga tatgcatatc cagggatttt ttgccaggtg gtaggagaga 540
ttat 544

<210> 430
<211> 507
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(507)

<223> n = A,T,C or G

<400> 430

cttatcncaa tggggctccc aaacttggct gtgcagtgga aactccgggg gaattttgaa 60
gaacactgac acccatettc caccggaca ctctgattta attggctgc agtgagaaca 120
gagcatcaat taaaaaagct gcccagaatg ttntcctggg cagcgttgt atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcataacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cnccctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcggtt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtgaa tggataatct aatgtgttcc tagtaggcac agggctccc gcccaggcct 420
cattctctc tggctctaa tagtcaatga ttgtgttagcc atgcctatca gtaaaaagat 480
tttgagcaa aaaaaaaaaa aaaaaaaaa 507

<210> 431

<211> 392

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 431

gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtatttattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtccctgggtt ttccaacaga 240
catcattcca gcattctgag attaggngaa ttggggatca ttctggagtt ggaatgttca 300
acaaaatgtga tgggtttagg taaaatgtac aacttctgga tctatgcaga cattgaagg 360
gcaatgagtc tggctttac tctgctgttt ct 392

<210> 432

<211> 387

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(387)

<223> n = A,T,C or G

<400> 432

ggtatccnta cataatcaaata tatacgta gtacatgtt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctttg tcttattctt ttgtctataa tactgtattt 120
ngtagtccaa gctctcggnna gtccagccac tggaaacat gctccctta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tattttgtt ctgtctgnng 240
attctgttgc ttctggggca ttcccttgng atgcagagga ccaccacaca gatgacagca 300
atctgaattt gtcataatcac agctgcgatt aagacataact gaaatcgatc aggaccggga 360
acaacgtata gaacactgga gtcctt 387

<210> 433

<211> 281

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(281)

<223> n = A,T,C or G

<400> 433

ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtgaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgttattac accagngagg ntctctgtnt gcccaactggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281

<210> 434

<211> 484

<212> DNA

<213> Homo sapiens

<400> 434

ttttaaaaata agcatttagt gctcagtccc tactgagtac tctttctctc ccctcctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcaactgtg atgtatattg 120
tgttgcaaaa aaaaaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
ttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatggttc tcagaaccat ttcacccaga 300
cagcctgttt ctatcctgtt taataaaatta gttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga ttgcaacata tgagtgtttt gaaaataaaag taccatgtc 420
ttta 484

<210> 435

<211> 424

<212> DNA

<213> Homo sapiens

<400> 435

gccccgcctca gagcagggtca ctttctgcct tccacgtcct cttcaagga agccccatgt 60
gggttagctt caatatcgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgccca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcaagcgac 180
atgggcctgt ggggagggggg caagatagat gagggggagc ggcatggtgc ggggtgaccc 240
cttggagaga gaaaaaaggc cacaagaggg gctgccaccc ccaactaacgg agatggccct 300
ggtagagacc tttgggggtc tggAACCTCT ggactccca tgctctaact cccacactct 360
gctatcagaa acttaaactt gaggatttc tctgttttc actcgcaata aattcagagc 420
aaac 424

<210> 436

<211> 667

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(667)

<223> n = A,T,C or G

<400> 436

acttggaa nactctcaca atataaaggc tcgttagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agcctcttctt ggaattcctc tgatttcaaa gtctcactct caagttcttgg aaaaagg 180
cagttectga aaggcaggta tagcaactga tcttcagaaa gaggactgt gtgcacccggg 240
atgggctgcc agatggat aggattccag atgctgacac ttctggggg aaacagggtc 300
gccagggttg tcatgact catcaaagtc cggtcaacgt ctgtgcttcg aatataaacc 360

tgttcatgtt tataggactc attcaagaat tttctataatc tctttcttat atactctcca 420
agttcataat gctgctccat gcccagctgg gtgagttggc caaatccttg tgccatgag 480
gattcctta tgggtcagt gggaaagggtg tcaatggac ttccgtctcc atgccgaaac 540
accaaaagtca caaacttcaa ctccctggct agtacacttc ggtctagcca gaaaaaaaaagc 600
agaaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tgttag 667

<210> 437

<211> 693

<212> DNA

<213> Homo sapiens

<400> 437

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cggttttgc 120
taaagctcag gtaggaggc tgataagctt ggaaggaact tcagacagct tttcagatc 180
ataaaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggtactcct ctatttcac ccctcttgct tctactctct ggcagtcaga cctgtggag 300
gccatggag aaaggagetc tctggatgtt tgtagacatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttggggggac agccagcatc tttagcttgc 420
atttgagttt ctgtctgtct tcagtagagg aaactttgc tttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tcctatttctt aggactgag ggctgtgggg taccttgcgtt tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgtt actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctaaaaatg acc 693

<210> 438

<211> 360

<212> DNA

<213> Homo sapiens

<400> 438

ctgcttatca caatgaatgt tctcctggc agcggtgtga tctttgccac cttcgtgact 60
ttatgcaatg catcatgcta tttcataacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaag acaactgcca aagaatctt aagaaggagg 180
actgcaagta tatctgtgtt agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tggcttctta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

<210> 439

<211> 431

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1) ... (431)

<223> n = A,T,C or G

<400> 439

gttcctnnta actcctgccca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaaggcctt agccttggct tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttgggt gtttcggcat ggagacccgaa 180
gtccccatga caccttccc actgacccca taaaggaatc ctcacgccca caaggatttg 240
gccaaactcac ccagctgggc atggagcagc attatgaact tggagagttt ataagaaaga 300
gatataaaaa attttgtat gaggcttata aacatgaaca gttttatatt cgaagcacag 360
acgttgaccg gactttgtat agtgctatga caaacctggc agccctgcga cgcggcccg 420
aatttagtag t 431

<210> 440
<211> 523
<212> DNA
<213> Homo sapiens

<400> 440
agagataaaag cttaggtcaa agttcataga gttccatga actatatgac tggccacaca 60
ggatctttt tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaatggaa cagattcaa aaaaaaaccc cacaatctag ggtggaaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agtttctcc 300
actggaaaac tgctactatc tgttttata ttctgttaa aatataatgag gctacagaac 360
taaaaattaa aaccttttg tgccttgg tcctggaaaca ttatgttcc tttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatacgca gctcttgaag 480
tatataatatc atagcaaata agtcatctga tgagaacaag cta 523

<210> 441
<211> 430
<212> DNA
<213> Homo sapiens

<400> 441
gttcctccta actcctgcc aaaaacgctc tcctcaacat gagagctgca cccctcctcc 60
tggccaggc agcaagcctt agccttggt tcttgttct gcttttttc tggcttagacc 120
gaagtgtact agccaaggag ttgaagttt tgactttggt gtttcggcat ggagaccgaa 180
gtccccattga caccttccc actgacccca taaaggaatc ctatggcca caaggattt 240
gccaactcac ccagctggc atggagcagc attatgaact tggagagttataaagaaaaga 300
gatataaaaa atttttgaat gagtcctata aacatgaaca gtttatatt cgaagcacag 360
acgttgaccg gactttgtatc agtgcatacgcaaaacgtggc agccctgtca cgccggcccg 420
aatttagtag 430

<210> 442
<211> 362
<212> DNA
<213> Homo sapiens

<400> 442
ctaaggaatt agtagtgttc ccatcacttg tttggagtgt gctattctaa aagattttga 60
tttcctggaa tgacaattat atttttaactt tgggggggaa aagagttata ggaccacagt 120
cttcacttct gatacttgc aattaatctt ttattgcact tttttgacc attaagctat 180
atgttttagaa atggtcattt tacggaaaaaa ttagaaaaat tctgataataa gtgcagaata 240
aatgaattaa tgtttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc 362

<210> 443
<211> 624
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(624)
<223> n = A,T,C or G

<400> 443
ttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60

ttgaaagaat taaaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgcattt taaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgcctttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaacttct attaacttgg ctccctgttt 300
tataaaatat tgtaataat atcacctact tcaaaggca gttatgaggc taaaatgaac 360
taacgcctac aaaacactta aacatagata acataggc aagtactatg tatctggcac 420
atggtaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtc atatgcta 480
agtacagaga gagggcactt aaaccaacta agggcctgga gggaaaggttt cctggaaaga 540
ngatgctgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatc 624

<210> 444
<211> 425
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(425)
<223> n = A,T,C or G

<400> 444
gcacatcatt nntcttgcat tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgtttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaaattgc ataagtggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagagggtgg taaaatcctt tgcacac tctaactccc tgaatgtttt 240
gctgtgtgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttggttt tgcacatcctgt gaagagccaa 360
ggagggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420
gtaga 425

<210> 445
<211> 414
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G

<400> 445
catgtttatg nttttggatt actttggca cctagtgttt ctaaatcgct tatcattctt 60
ttctgtttt caaaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaaattctt tgcattgtggc agattattgg atgtatgtt ctttaactag catataaaatc 180
tggtgtgttt cagataaaatg aacagaaaaa tgggtggaa ttaccatttg gacattgtg 240
aatgaaaaat tggtcctcta gattatgtaa caaataacta tttcctaacc attgatctt 300
ggattttat aatcttactc acaaattgact aggcttctcc tcttgtattt tgaagcagtg 360
tgggtgtgg attgataaaa aaaaaaaaaa tcgacgcggc cgcaattta gtag 414

<210> 446
<211> 631
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(631)

<223> n = A,T,C or G

<400> 446

acaaattaga anaaagtgc agagaacacc acatacctt tccggAACat tacaatggct 60
tctgcatca tgggaAGTgt gggcattcta tcaatATGca ggagccatct tgCAGGTgt 120
atgCTGGta tactggacaa cactgtgaaa aaaaggacta cagtgtctA tacgttggc 180
ccggTCCTgt acgatttcag tatgtctta tcgcagctgt gattggAACa attcagattg 240
ctgtcatctg tgggtggc ctctgcatca caagggccaa actttAGGta atagcattgg 300
actgagattt gtaaacttcc caaccttcca ggAAATGCCc cagaAGCAAC agaATTcaca 360
gacagaAGCA aaatacaggg cactacAGt cagacaatac aacaAGAGCG tccACGAGGT 420
taatctaaAG ggAGCATGTT tcacAGTggc tggACTACCG agagCTTggA ctacacaata 480
cagtattata gacaaaAGAA taagACAAGA gatctACACA tggTCCTG catttGTTG 540
aatctacACC aatgAAAACA tggACTACAG ctatATTGA ttatgtatgg atatATTGA 600
aatAGTATAc attgtctGA tggTTTtct g 631

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

ccttggggaaa antntcacaa tataaAGGgt cgtagacttt actccAAatt ccaAAAGgt 60
cctggccatg taatcctgaa agtttccca aggtAGCTat AAAATCCTA taagggtgca 120
gccttcttg gaattcctct gatttcaaAG tctcaCTC aagttcttga aaACGAGGGC 180
agttcctgaa aggCAGGTat agcaACTGat ctTCAGAAAG aggaACTGtG tgCACCGGGA 240
tgggCTGCCa gagTAGGATA ggattCCAGA tgCTGACACC ttCTGGGGGA AACAGGGCTG 300
ccaggtttgt catAGCACTC atCAAAGTCC ggtcaACGTC tggTCTCgA atataAAACt 360
gttcatgttt ataggactca ttcaAGAATT ttCTATATCT ctTTCTTATA tactCTCCAA 420
gttcatatagt ctgCTCCATG CCCAGCTGGG tgAGTTGGCC AAATCCTGT ggCCATGAGG 480
attcCTTtat ggggtcAGTg ggAAAGGTgt caatGGACT tcggTCTCCA tgCCGAAACA 540
ccaaAGTCAC aaACTTCAAC tcCTTGGCTA gtACACTTCG gtCTA 585

<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

tgcTGTGGG tcattctgan nnccGAactg accNTGCCAG ccCTGCCGAN gggCCnCCat 60
ggCTCCCTAG tgCCCTGGAG aggANGGGC tag 93

<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1) ... (706)
<223> n = A,T,C or G

<400> 449

ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnntgc tcgtgggtca 60
ttctgancac cgaactgacc atgccagccc tgccgatggc cctccatggc tccttagtgc 120
cctggagagg aggtgtctag tcagagagta gtccttggaaag gtggcctctg ngaggagcca 180
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caactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcnccccca 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaaa 706

<210> 450

<211> 493

<212> DNA

<213> Homo sapiens

<400> 450

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acagtttaa aaggtaaaac aacataaaaaa gaaatatcct atagtggaaa taagagagtc 120
aatatgaggct gagaacttta caaaggatc ttacagacat gtcgccaata tcactgcac 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcaggt agtggaaatgg gtggaaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagtggat ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac-acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagcttac aaactccat tgccgagggt cgacgcggcc 480
gcgaatttag tag 493

<210> 451

<211> 501

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1) ... (501)

<223> n = A,T,C or G

<400> 451

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ctttcgcta ttacgcccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg tttcccagt cnccacgttg taaaacgacg gccagtaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgccgc cgcgctcgacg tggatccnc actgagagag 300
tggagagtga catgtgttgg acnctgttca tgaaggactg agcagaagct ggaggcaca 360
cgcnccagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggccnctgcn ccccagcatg gatgacagag taaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501

<210> 452

<211> 51

<212> DNA

<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(51)
<223> n = A,T,C or G

<400> 452
agacggtttc accnttacaa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453
<211> 317
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(317)
<223> n = A,T,C or G

<400> 453
tacatctgc ttttccccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60
acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatggttc tcagaaccat 120
ttcacccana cagcctgttt ctatcctgtt taataaattta gtttgggttc tctacatgca 180
taacaaacccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
cccaccaaac tttatTTTC tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
tacccatgtc tttatta 317

<210> 454
<211> 231
<212> DNA
<213> Homo sapiens

<400> 454
ttcgaggtagt aatcaactct cagagtgttag tttccttcta tagatgagtc agcattaata 60
taagccacgc cacgctcttg aaggagtctt gaattctcct ctgctcactc agtagaaacca 120
agaagaccaa attcttctgc atcccagttt gcaaacaaaa ttgttcttctt aggtctccac 180
ccttccttt tcagtggtcc aaagctcctc acaatttcat gaacaacagc t 231

<210> 455
<211> 231
<212> DNA
<213> Homo sapiens

<400> 455
taccaaagag ggcataataa tcagtctcac agtagggttc accatcctcc aagtggaaaa 60
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
gtttcaacgc attgatgact tctccaagga tcttccttt gcacatcgacca cattcagggg 180
caaagaattt ctcatagcac agtcacaaat acagggtcc tttctcctct a 231

<210> 456
<211> 231
<212> DNA
<213> Homo sapiens

<400> 456
ttggcaggta cccttacaaa gaagacacca taccttatgc gttatttaggt ggaataatca 60
ttccatttcag tattatcggtt attattcttg gagaaaacct gtctgtttac tgtaaccttt 120
tgcactcaaa ttcctttatc aggaataact acatagccac tatttacaaa gccattggaa 180

ccttttatt tggtcagct gctagtcagt ccctgactga cattgccaag t 231

<210> 457
<211> 231
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A,T,C or G

<400> 457
cgaggtaccc aggggtctga aaatctctnn tttantagtc gatagcaaaa ttgttcatca 60
gcattcccta atatgatctt gctataatta gatffffctc cattagagtt catacagttt 120
tatttgattt tatttagcaat ctcttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggctttgt g 231

<210> 458
<211> 231
<212> DNA
<213> Homo sapiens

<400> 458
aggtctgggtt ccccccactt ccactccccct ctactctctc taggactggg ctggggccaag 60
agaagaggggg tggtaggga agccgttgag acctgaagcc ccaccctcta ctttccttca 120
acacccttaac ctggggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180
ggtcctgggt taggcatttt gggggccag accccaggag aagaagattc t 231

<210> 459
<211> 231
<212> DNA
<213> Homo sapiens

<400> 459
ggtaccgagg ctcgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
cttcgcgaa acctgtgggtg gcccaccagt cctaacggga caggacagag agacagagca 120
ccctgcact gtttccctc caccacagcc atcctgtccc tcattgtc tcattgtc 180
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231

<210> 460
<211> 231
<212> DNA
<213> Homo sapiens

<400> 460
gcaggtataa catgctgcaa caacagatgt gacttaggaac ggccgggtgac atggggaggg 60
cctatcaccc tatttttggg ggctgcttct tcacagtgtat catgaagcct agcagcaa 120
cccacccccc cacacgcaca cggccagcct ggagccaca gaagggtcct cctgcagcca 180
gtggagcttg gtccagcctc cagtcaccc ctaccaggct taaggataga a 231

<210> 461
<211> 231
<212> DNA
<213> Homo sapiens

<400> 461
cgaggttga gaagctctaa tgtgcagggg agccgagaag caggcgccct agggagggtc 60

gcgtgtgctc cagaagagtg tgcgtatgcc agagggaaa caggcgctg tgtgtcctgg 120
gtgggttca gtgaggagtg ggaaatttgt tcagcagaac caagccgtg ggtgaataag 180
agggggatc catggactg atagagccct atagtttcag agctggaaat t 231

<210> 462
<211> 231
<212> DNA
<213> Homo sapiens

<400> 462
aggtaaccctc atttagcca tggaaaaatt gatgttcagt ggggatcagt gaattaaatg 60
gggtcatgca agtataaaaa ttaaaaaaaaa aagacttcat gcccaatctc atatgtatgtg 120
gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180
tctagaggag gtatTTAATT tcttctact catccagtgt tgtatTTAGG a 231

<210> 463
<211> 231
<212> DNA
<213> Homo sapiens

<400> 463
tactccagcc tggcacaca gcgagaccct atcacccccc cccacccac caaaaaaaaaa 60
actgagtaga cagggtcct ctggcatgg taagtcttaa gtccccccc agatctgtga 120
catttgacag gtgttttc ctctggacct cggtgtcccc atctgagtga gaaaaggcag 180
tggggaggtg gatcttccag tcgaagccggt atagaagccc gtgtgaaaag c 231

<210> 464
<211> 231
<212> DNA
<213> Homo sapiens

<400> 464
gtactctaag atttatcta agttgcctt tctgggtggg aaagtttaac ctttagtgact 60
aaggacatca catatgaaga atgtttaagt tggaggtggc aacgtgaatt gcaaacaggg 120
cctgcttcag tgactgtgtg cctgttagtcc cagctactcg ggagtctgtg tgaggccagg 180
gtgtccagcg caccagctag atgctctgta acttcttaggc cccatTTCC c 231

<210> 465
<211> 231
<212> DNA
<213> Homo sapiens

<400> 465
catgttggtg tagctgtggt aatgctggct gcacatcaga cagggttaac ttcaagctcct 60
gtggcaaaatt agcaacaaat tctgacatca tattttatggt ttctgtatct ttgttcatgt 120
aggatggcac aatttttgc tggatcata atataactcg attagttcag ctccatcaga 180
taaaactggag acatgcagga cattaggta gtgtttagc tctggtaatg a 231

<210> 466
<211> 231
<212> DNA
<213> Homo sapiens

<400> 466
caggtaccc tttccattgg atactgtgct agcaagcatg ctctccgggg ttttttaat 60
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cctgtgcaat caaatattgt ggagaattcc ctagctggag aagtccacaaa gactataggc 180
aataatggag accagtcggccca caagatgaca accagtcgtt gtgtgcggct g 231

<210> 467
<211> 311
<212> DNA
<213> Homo sapiens

<400> 467
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tgtgccttaa cagaaggctt tgagattcta agtggaaatc atttcagtga ctgtcatgtg 180
gcatgggtct ctgcccaggc tcgtaatgag actatagcaa ggccggctgtg ggacgtcagt 240
tgtgacctgc tggcctccc aatagactaa caggcagtgc cagttggacc caagagaaga 300
ctgcagcaga c 311

<210> 468
<211> 3112
<212> DNA
<213> Homo sapiens

<400> 468
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aagatctgca tgggtggaaag gacctgtatga tacagatgtt gataggagac aattaaaggc 120
tggaggcac tggatgcctg atgatgaagt ggactttcaa actggggcac tactgaaaacg 180
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 tgagtgcgt ttagaatttt ggcaaatcat actggtaact tatctcaact ttgagatgtg 3000
 tttgtccctt tagttaattt aaagaaatag ggcaactctt tgagccactt tagggttcac 3060
 tcctggcaat aaagaattt caaagagcaa aaaaaaaaaa aaaaaaaaaa aa 3112

<210> 469

<211> 2229

<212> DNA

<213> Homo sapiens

<400> 469

agcttttgtt aaattcttta ttgccaggag tgaaccctaa agtggctcac aagagtgc 60
 tatttcttc aattaactac aaggacaaac acatctcaa gttgagataa gtgaccagta 120
 tgatttgcca aaattctaaa gcgcactcac catgaaatgg ataaaggta ctttgggg 180
 tttgcactgc atgaattctg taaaaagttt gttggatatt gtgatagaga tagagaaatg 240
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 ggtcacctga ggtcaggatg tcaagaccag cctggccat atggtaaagcc cccatctca 2160
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aatggaatt 2229

<210> 470

<211> 2426

<212> DNA

<213> Homo sapiens

<400> 470

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 gcatgaattc tgtaaaaagc ttgttggata ttgtgataga gatagagaaa tgaagtatat 240
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 ccataaaacat tccctctgtg gctcttgcat ttcatatatt tatctaaact ctataatca 360
 aattacaett ttagtatttgc ctgtctcatg tgatgatgaa tctcatatgt gtcccttctt 420
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<211> 812

<212> DNA

<213> Homo sapiens

<400> 471

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<211> 515

<212> DNA

<213> Homo sapiens

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<400> 472

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<210> 473

<211> 5829

<212> DNA

<213> Homo sapiens

<400> 473

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<211> 1594

<212> DNA

<213> Homo sapiens

<400> 474

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<211> 2414
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> (33)
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<400> 475

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<211> 3434
<212> DNA
<213> Homo sapiens

<400> 476

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<210> 477

<211> 140

<212> PRT

<213> Homo sapiens

<400> 477

Met Asp Gly His Thr Asp Ile Trp Arg Asn His Met Asp Thr Pro Pro
5 10 15

His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His Met Asp Thr
20 25 30

Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
35 40 45

His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
50 55 60

His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
65 70 75 80

Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
85 90 95

Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr
100 105 110

Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val
115 120 125

Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln
130 135 140

<210> 478

<211> 143

<212> PRT

<213> Homo sapiens

<400> 478

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
5 10 15

Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
20 25 30

Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr
35 40 45

His Gly Asp Ile Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
65 70 75 80

Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
85 90 95

His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp
100 105 110

Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
115 120 125

His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
130 135 140

<210> 479

<211> 222

<212> PRT

<213> Homo sapiens

<400> 479

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
5 10 15

Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
20 25 30

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr
35 40 45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
65 70 75 80

Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser
85 90 95

His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val
100 105 110

Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val
115 120 125

Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr
130 135 140

Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His
145 150 155 160

Cys His Thr Asp Thr Thr Ser Leu Pro His Phe His Val Ser Ala
165 170 175

Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp
180 185 190

Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala
195 200 205

Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val
210 215 220

<210> 480
<211> 144
<212> PRT
<213> Homo sapiens

<400> 480
Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val
5 10 15
Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr
20 25 30
Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg
35 40 45
Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly
50 55 60
Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln
65 70 75 80
Asp Arg Leu Thr Trp Ser Ser Val Ala Gly Val Cys Ala Cys
85 90 95
Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly
100 105 110
Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu
115 120 125
Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly
130 135 140

<210> 481
<211> 167
<212> PRT
<213> Homo sapiens

<400> 481
Met His Gly Pro Gln Val Leu Ala Arg Cys Ser Glu Cys Ala Cys Pro
5 10 15
Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg
20 25 30
Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser
35 40 45
Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys
50 55 60
Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro

65	70	75	80
Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser Ser Trp Arg			
85	90	95	
Ala Leu Ala Glu Val Thr Gly Cys Ser Leu Gly Pro Leu Gly Leu Ala			
100	105	110	
Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys Trp Ser His			
115	120	125	
Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr Ala Ala Phe			
130	135	140	
Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu Trp Ala Ser			
145	150	155	160
Trp Leu Ser Arg Gly Arg Pro			
165			

<210> 482
<211> 143
<212> PRT
<213> Homo sapiens

<400> 482			
Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val			
5	10	15	
Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu			
20	25	30	
Arg Ala Ser Trp Leu Pro Gly Gly Pro Gln Ala Ile Leu Gly Arg			
35	40	45	
Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly			
50	55	60	
Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe			
65	70	75	80
Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr			
85	90	95	
Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly			
100	105	110	
Ala Ser Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys			
115	120	125	
Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly			
130	135	140	

<210> 483
<211> 143
<212> PRT

<223> Made in a lab

<400> 486
gcgaattctc acgctgagta tttggcc 27

<210> 487
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 487
cccgaaattct tagctgccca tccgaacgcc ttcatc 36

<210> 488
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 488
gggaagcttc ttccccggct gcaccagctg tgc 33

<210> 489
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 489
Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
1 5 10 15
Ser Val Ala

<210> 490
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 490
Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
1 5 10 15
Leu Ser His Ser
20

<210> 491
<211> 20
<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 491

Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
1 5 10 15

Thr Gly Phe Thr
20

<210> 492

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 492

Ala Leu Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr
1 5 10 15

Leu Ala Ser Leu
20

<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

Tyr Thr Leu Ala Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro
1 5 10 15

Lys Tyr Arg Gly
20

<210> 494

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 494

Leu Pro Lys Tyr Arg Gly Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser
1 5 10 15

Leu Met Ile Ser
20

<210> 495

<211> 20

<212> PRT

<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 495
Asp Ser Leu Met Thr Ser Phe Leu Pro Gly Pro Lys Pro Gly Ala Pro
1 5 10 15
Phe Pro Asn Gly
20

<210> 496
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 496
Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
1 5 10 15
Pro Pro Pro Pro Ala
20

<210> 497
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 497
Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val
1 5 10 15
Ser Val Arg Val
20

<210> 498
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 498
Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val
1 5 10 15
Val Pro Gly Arg
20

<210> 499
<211> 20
<212> PRT
<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 499

Arg	Val	Val	Pro	Gly	Arg	Gly	Ile	Cys	Leu	Asp	Leu	Ala	Ile	Leu	Asp
1					5				10				15		
Ser	Ala	Phe	Leu												
					20										

<210> 500

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 500

Leu	Asp	Ser	Ala	Phe	Leu	Leu	Ser	Gln	Val	Ala	Pro	Ser	Leu	Phe	Met
1					5				10				15		
Gly	Ser	Ile	Val												
					20										

<210> 501

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 501

Phe	Met	Gly	Ser	Ile	Val	Gln	Leu	Ser	Gln	Ser	Val	Thr	Ala	Tyr	Met
1					5				10			15			
Val	Ser	Ala	Ala												
					20										

<210> 502

<211> 414

<212> DNA

<213> Homo Sapien

<220>

<221> misc_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 502

caccatggag	acaggcctgc	gctggctttt	cctggtcgct	gtgctcaaag	gtgtccaatg	60
tcagtcggtg	gaggagtccg	ggggtcgcct	ggtcacgcct	gggacacctt	tgacantcac	120
ctgttagagtt	tttggaatng	acctcagtag	caatgcaatg	agctgggtcc	gccaggctcc	180
agggaaagggg	cttggaatgga	tggagccat	tgataattgt	ccacantacg	cgacctgggc	240
gaaaggccga	ttnatnattt	ccaaaacctn	gaccacgggt	gatttgaaaa	tgaccagtcc	300
gacaaccgag	gacacggcca	cctatTTTG	tggcagaatg	aatactggta	atagtggttg	360
gaagaatatt	tggggcccag	gcaccctgggt	caccgtntcc	tcagggcaac	ctaa	414

<210> 503

<211> 379

<212> DNA

<213> Homo Sapiens

<220>

<221> misc_feature

<222> (1)...(379)

<223> n = A,T,C or G

<400> 503

atncgatgg	gttggtcaa	agggtccag	tgtcagtccgg	tggaggagtc	cgggggtcg	60
ctggcacgc	ctgggacacc	cctgacactc	acctgcaccc	tntctggatt	ngacatcagt	120
agctatggag	tgagctgggt	ccgccaggct	ccagggaaagg	ggctgnata	catcgatca	180
ttagtagtag	tgttacattt	tacgcagct	gggcgaaagg	ccgattcacc	atttccaaaa	240
cctngaccac	ggtggatttg	aaaatcacca	gtttgacaac	cgaggacacg	gccacctatt	300
tntgtgccag	aggggggtt	aattataaag	acatttgggg	cccaggcacc	ctggtcacccg	360
tntccttagg	gcaacctaa					379

<210> 504

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 504

Gly	Phe	Thr	Asn	Tyr	Thr	Asp	Phe	Glu	Asp	Ser	Pro	Tyr	Phe	Lys	Glu
1				5				10				15			
Asn Ser Ala															

<210> 505

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 505

Lys	Glu	Asn	Ser	Ala	Phe	Pro	Pro	Phe	Cys	Cys	Asn	Asp	Asn	Val	Thr
1				5				10				15			
Asn Thr Ala Asn															
				20											

<210> 506

<211> 407

<212> DNA

<213> Homo Sapien

<400> 506

atggagacag	gcctgcgctg	gttctccctg	gtcgctgcgc	tcaaagggt	ccagtgtcag	60
tcgctggagg	agtccggggg	tcgcctggtc	acgcctggga	cacccctgac	actcacctgc	120
accgtctctg	gattctccct	cagtagaat	gcaatgatct	gggtccgcca	ggctccaggg	180
aaggggctgg	aatacatcg	atacattagt	tatggtggt	gcmcatacta	cgcgagctgg	240
gtgaaaggcc	gattcaccat	ctccaaaacc	tcgaccacgg	tggatctgag	aatgaccagt	300
ctgacaaccg	aggacacggc	cacctatttc	tgtgccagaa	atagtgattt	tagtggatg	360
ttgtgggccc	caggcaccct	ggtcaccg	tcctcaggc	aacctaa		407

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<210> 507
<211> 422
<212> DNA
<213> Homo Sapien

<400> 507
atggagacag gcctgcgtcg gttctcctg gtcgtgtgc tcaaagggtgt ccagtgtcag
tcgggtggagg agtccggggg tcgcctggtc acgcctggga caccctgac actcacctgt
acagtctctg gattctccct cagcaactac gacctaact gggtccgcca ggctccaggg
aaggggctgg aatggatcggtatcatataat tatgttggta ggacggacta cgcaactgg
gcaaaaaggcc ggttcacccat ctccaaaacc tcgaccaccc tggatctcaa gatcgccagt
ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaaagtg cgatgagtct
ggtccgtgct tgccatctg gggcccaggc accctggtca ccgtctcctt agggcaacct
aa

<210> 508
<211> 411
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (1)...(411)
<223> n = A,T,C or G

<400> 508
atggagacag gcctcgctgg cttctcctgg tcgctgtgct caaagggtgtc cagtgtcagt
cggtggagga gtccgggggt cgccctggta cgccctgggac acccctgaca ctcacctgca
cagtctctgg aatcgaccc tcgactact gcatgagctg ggtccggccag gtcggaggaa
aggggctgg aatggatcggtatcatataat ttggta ctccctggta cacataactac gcgaggtggg
cgaaaaggccg attcaccatc tccaaaacct cgaccacggg gcatntgaaa atcnccagtc
cgacaaccga ggacacggc acctatttc gtgccagaga tcttcggat ggttagtagta
ctggttatta taaaatctgg gggccaggca ccctggtca cgtctcctt g

<210> 509
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 509
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
1 5 10 15

<210> 510
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 510
Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile
1 5 10 15

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<210> 511
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys
1 5 10 15

<210> 512
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 512

Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu
1 5 10 15

<210> 513
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 513

Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu
1 5 10 15

<210> 514
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 514

Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
1 5 10 15

<210> 515
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 515
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg
1 5 10 15

<210> 516
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 516
Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln
1 5 10 15

<210> 517
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 517
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met
1 5 10 15

<210> 518
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 518
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
1 5 10 15

<210> 519
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 519
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys
1 5 10 15
Gly

<210> 520
<211> 25
<212> PRT
<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 520

Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
1 5 10 15
Glu Ala Arg Arg His Tyr Asp Glu Gly
20 25

<210> 521

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 521

Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
1 5 10 15
Pro Pro Pro Pro Ala
20

<210> 522

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 522

Leu Leu Val Val Pro Ala Ile Lys Lys Asp Tyr Gly Ser Gln Glu Asp
1 5 10 15
Phe Thr Gln Val
20

<210> 523

<211> 254

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<220>

<221> VARIANT

<222> (1)...(254)

<223> Xaa = any amino acid

<400> 523

Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
1 5 10 15
Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
20 25 30
Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
35 40 45

Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
 50 55 60
 Trp Val Leu Ser Ala Thr His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
 65 70 75 80
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
 85 90 95
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
 100 105 110
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
 115 120 125
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
 130 135 140
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
 145 150 155 160
 Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
 165 170 175
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
 180 185 190
 Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly
 195 200 205
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
 210 215 220
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
 225 230 235 240
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 245 250

<210> 524

<211> 765

<212> DNA

<213> Homo sapien

<400> 524	524
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<210> 525

<211> 254

<212> PRT

<213> Homo sapien

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Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu	

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Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val	Leu Val His Pro Gln	
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Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn	Ser Tyr Thr Ile Gly	
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Leu Gly Leu His Ser Leu Glu Ala Asp Gln	Glu Pro Gly Ser Gln Met	
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Val Glu Ala Ser Leu Ser Val Arg His Pro Glu	Tyr Asn Arg Pro Leu	
100	105	110
Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp	Glu Ser Val Ser Glu	
115	120	125
Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser	Gln Cys Pro Thr Ala	
130	135	140
Gly Asn Ser Cys Leu Val Ser Gly Trp Gly	Leu Leu Ala Asn Gly Arg	
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Met Pro Thr Val Leu Gln Cys Val Asn Val	Ser Val Val Ser Glu Glu	
165	170	175
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His	Pro Ser Met Phe Cys	
180	185	190
Ala Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn	Gly Asp Ser Gly	
195	200	205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly	Leu Val Ser Phe Gly	
210	215	220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro	Gly Val Tyr Thr Asn Leu	
225	230	235
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<210> 526

<211> 963

<212> DNA

<213> Homo sapiens

<400> 526

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<211> 320

<212> PRT

<213> Homo sapiens

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Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met
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Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile
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Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Phe Glu Ala Cys
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Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr
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Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro
115 120 125

Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly
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Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Pro Leu Pro Leu
145 150 155 160

Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser
165 170 175

Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu
180 185 190

Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val
195 200 205

Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val
210 215 220

Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys
225 230 235 240

Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly
245 250 255

Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg
260 265 270

Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro
275 280 285

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305

310

315

320

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 <213> Homo Sapien

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<400> 529
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<210> 530
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 <212> DNA
 <213> Homo sapiens

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 <211> 879

<212> DNA

<213> Homo sapiens

<400> 531

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<211> 292

<212> PRT

<213> Homo sapiens

<400> 532

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Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe							
35	40	45					

Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp							
50	55	60					

Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu							
65	70	75	80				

Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg							
85	90	95					

Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp							
100	105	110					

Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser							
115	120	125					

Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu							
130	135	140					

Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu							
145	150	155	160				

Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile							
165	170	175					

Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu
180 185 190

Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu
195 200 205

Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu
210 215 220

Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu
225 230 235 240

Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys
245 250 255

Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp
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Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu
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Val Ile Ile Met
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<213> *Homo sapiens*

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 35 40 45
 Ala Lys Arg Pro Thr Thr Gly His Leu Glu Lys Glu Phe Met Phe His
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 Cys Arg Lys Gln Pro Gly Ser Pro Ser Arg Gly Leu Gly Leu Leu Trp
 65 70 75 80
 Pro Trp Pro Asp Ile Glu Phe Val Pro Arg Gln Asp Lys Leu Thr Gln
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 Ser Ser Val Leu Val Pro Gln Ile Cys Ala Cys Gln Thr Arg Pro Asn
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 Trp Leu Asn Glu Gln Pro Ala Thr Ser Ala Gly Val Arg Leu Glu Glu
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 Val Asp Gln Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys
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 180 185 190
 Ser Trp His Thr Leu Ala Glu Val Thr Gly Cys Ser Leu Ser Pro Leu
 195 200 205
 Ser Leu Ala Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys
 210 215 220
 Trp Ser His Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr
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<210> 535
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 <212> DNA
 <213> Homo sapiens

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Ile Gly His Lys Arg Arg Leu Glu Glu Asp Asp Met Tyr Ser Val Leu
 35 40 45

Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu Leu Gln Gly Phe Trp
 50 55 60

Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala Gln Lys Pro Ser Leu

65

70

75

80

Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser Tyr Leu Val Leu Gly
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Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val Ile Gln Pro Ile Phe
 100 105 110

Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr Asp Pro Met Asp Ser
 115 120 125

Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr Val Leu Thr Phe Cys
 130 135 140

Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr Phe Tyr His Val Gln
 145 150 155 160

Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys His Met Ile Tyr Arg
 165 170 175

Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly Lys Thr Thr Gly
 180 185 190

Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn Lys Phe Asp Gln Val
 195 200 205

Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro Leu Gln Ala Ile Ala
 210 215 220

Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile Ser Cys Leu Ala Gly
 225 230 235 240

Met Ala Val Leu Ile Ile Leu Pro Leu Gln Ser Cys Phe Gly Lys
 245 250 255

Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr Phe Thr Asp Ala Arg
 260 265 270

Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile Arg Ile Ile Lys Met
 275 280 285

Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile Thr Asn Leu Arg Lys
 290 295 300

Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys Leu Arg Gly Met Asn
 305 310 315 320

Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile Val Phe Val Thr Phe
 325 330 335

Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr Ala Ser Arg Val Phe
 340 345 350

Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu Thr Val Thr Leu Phe
 355 360 365

Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg
 370 375 380

Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg
385 390 395 400

Gln Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr
405 410 415

Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser
420 425 430

Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly
435 440 445

Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro
450 455 460

Ser His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln
465 470 475 480

Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly
485 490 495

Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala
500 505 510

Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile
515 520 525

Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn
530 535 540

Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp
545 550 555 560

Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu
565 570 575

Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His
580 585 590

Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp
595 600 605

Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly
610 615 620

Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln
625 630 635 640

Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu
645 650 655

Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly
660 665 670

Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu
675 680 685

Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr
690 695 700

Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Leu
705 710 715 720

Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln Asp Trp Trp Leu Ser
725 730 735

Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val Thr Val Asn Gly Gly
740 745 750

Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp Tyr Leu Gly Ile Tyr
755 760 765

Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly Ile Ala Arg Ser Leu
770 775 780

Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln Thr Leu His Asn Lys
785 790 795 800

Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu Phe Phe Asp Arg Asn
805 810 815

Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys Asp Ile Gly His Leu
820 825 830

Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe Ile Gln Thr Leu Leu
835 840 845

Gln Val Val Gly Val Val Ser Val Ala Val Ala Val Ile Pro Trp Ile
850 855 860

Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe Ile Phe Leu Arg Arg
865 870 875 880

Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg Leu Glu Ser Thr Thr
885 890 895

Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser Leu Gln Gly Leu Trp
900 905 910

Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys Gln Glu Leu Phe Asp
915 920 925

Ala His Gln Asp Leu His Ser Glu Ala Trp Phe Leu Phe Leu Thr Thr
930 935 940

Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile Cys Ala Met Phe Val
945 950 955 960

Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala Lys Thr Leu Asp Ala
965 970 975

Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu Thr Leu Met Gly Met
980 985 990

Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val Glu Asn Met Met Ile

995

1000

1005

Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu Glu Lys Glu Ala Pro
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Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp Pro His Glu Gly Val
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Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser Pro Gly Gly Pro Leu
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Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser Gln Glu Lys Val Gly
 1060 1065 1070

Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser Leu Ile Ser Ala Leu
 1075 1080 1085

Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp Ile Asp Lys Ile Leu
 1090 1095 1100

Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile
 1105 1110 1115 1120

Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met Arg Lys Asn Leu Asp
 1125 1130 1135

Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu
 1140 1145 1150

Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro Gly Lys Met Asp Thr
 1155 1160 1165

Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val Gly Gln Arg Gln Leu
 1170 1175 1180

Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn Gln Ile Leu Ile Ile
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<212> PRT

<213> Homo sapiens

<400> 538

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Gln Lys Pro Ser Leu Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser
 35 40 45

Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val
 50 55 60

Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr
 65 70 75 80

Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr
 85 90 95

Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr
 100 105 110

Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys
 115 120 125

His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly
 130 135 140

Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn
 145 150 155 160

Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro
 165 170 175

Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile
 180 185 190

Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln
 195 200 205

Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr
 210 215 220

Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile
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Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile
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Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys
 260 265 270

Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile
 275 280 285

Val Phe Val Thr Phe Thr Tyr Val Leu Leu Gly Ser Val Ile Thr
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Ala Ser Arg Val Phe Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu
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Thr Val Thr Leu Phe Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala
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Ile Val Ser Ile Arg Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile
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Ser Gln Arg Asn Arg Gln Leu Pro Ser Asp Gly Lys Met Val His
355 360 365

Val Gln Asp Phe Thr Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr
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Leu Gln Gly Leu Ser Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val
385 390 395 400

Val Gly Pro Val Gly Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu
405 410 415

Gly Glu Leu Ala Pro Ser His Gly Leu Val Ser Val His Gly Arg Ile
420 425 430

Ala Tyr Val Ser Gln Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser
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Asn Ile Leu Phe Gly Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val
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Ile Lys Ala Cys Ala Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly
465 470 475 480

Asp Leu Thr Val Ile Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln
485 490 495

Lys Ala Arg Val Asn Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile
500 505 510

Tyr Leu Leu Asp Asp Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg
515 520 525

His Leu Phe Glu Leu Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr
530 535 540

Ile Leu Val Thr His Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile
545 550 555 560

Leu Ile Leu Lys Asp Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu
565 570 575

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580 585 590

Glu Glu Ser Glu Gln Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn
595 600 605

Arg Thr Phe Ser Glu Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro
610 615 620

Ser Leu Lys Asp Gly Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro
625 630 635 640

Val Thr Leu Ser Glu Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln
645 650 655

Ala Tyr Lys Asn Tyr Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile

660	665	670
Phe Leu Ile Leu Leu Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln		
675	680	685
Asp Trp Trp Leu Ser Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val		
690	695	700
Thr Val Asn Gly Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp		
705	710	715
Tyr Leu Gly Ile Tyr Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly		
725	730	735
Ile Ala Arg Ser Leu Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln		
740	745	750
Thr Leu His Asn Lys Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu		
755	760	765
Phe Phe Asp Arg Asn Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys		
770	775	780
Asp Ile Gly His Leu Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe		
785	790	795
Ile Gln Thr Leu Leu Gln Val Val Gly Val Val Ser Val Ala Val Ala		
805	810	815
Val Ile Pro Trp Ile Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe		
820	825	830
Ile Phe Leu Arg Arg Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg		
835	840	845
Leu Glu Ser Thr Thr Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser		
850	855	860
Leu Gln Gly Leu Trp Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys		
865	870	875
Gln Glu Leu Phe Asp Ala His Gln Asp Leu His Ser Glu Ala Trp Phe		
885	890	895
Leu Phe Leu Thr Thr Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile		
900	905	910
Cys Ala Met Phe Val Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala		
915	920	925
Lys Thr Leu Asp Ala Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu		
930	935	940
Thr Leu Met Gly Met Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val		
945	950	955
Glu Asn Met Met Ile Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu		
965	970	975

Glu Lys Glu Ala Pro Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp
980 985 990

Pro His Glu Gly Val Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser
995 1000 1005

Pro Gly Gly Pro Leu Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser
1010 1015 1020

Gln Glu Lys Val Gly Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser
1025 1030 1035 1040

Leu Ile Ser Ala Leu Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp
1045 1050 1055

Ile Asp Lys Ile Leu Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys
1060 1065 1070

Lys Met Ser Ile Ile Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met
1075 1080 1085

Arg Lys Asn Leu Asp Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp
1090 1095 1100

Asn Ala Leu Gln Glu Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro
1105 1110 1115 1120

Gly Lys Met Asp Thr Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val
1125 1130 1135

Gly Gln Arg Gln Leu Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn
1140 1145 1150

Gln Ile Leu Ile Ile Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr
1155 1160 1165

Asp Glu Leu Ile Gln Lys Lys Ile Arg Glu Lys Phe Ala His Cys Thr
1170 1175 1180

Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys
1185 1190 1195 1200

Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr
1205 1210 1215

Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln
1220 1225 1230

Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg
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Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser
1250 1255 1260

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Cys Leu Ser His Ser Val Ala Val Val Thr
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Ala Val Val Thr Ala Ser Ala Ala Leu
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Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu
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Thr Gln Val Val Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala
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<213> Homo sapiens

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Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe

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15

Met Thr

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Ser Val

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5 10 15Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met
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Val Ala Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu
5 10 15Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu
20 25 30Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys
35 40 45Cys Arg Met Pro Arg Thr Leu Arg Arg Leu
50 55

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Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu

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10

15

Glu Cys

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Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg
5 10 15

Gln Ala

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Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala
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